



1/28

Sal I Bam H I

| |
----- pUC 19

Xba I

1 ATGGAGTCAA AGTTTGCTCA CATCATTGTT TTCTTCTTC TTGCAACTTC
original sequence - ag a
51 CTTTGA~~AA~~CT CTCTGGCAC GAAAAGAAAG Tgatggacca gagatcttag
mutagenic primer
101 aacTTCAAAA GGAATTGAA TGCAATGGAA AACAAAGGTG GCCAGAACCTT
151 ATTGGTGTAC CAACAAAGCT TGCTAAGGGG ATAATTGAGA AGGAAAATTC
201 ACTCATAACT AATGTTCAGA TACTACTGAA TGGTTCTCCA GTCACAATGG
251 ATTATCGTTG TAATCGAGTT CGTCTTTTG ATAACATTAA GGGTGATGTT
301 GTACAAATTG CTAGGGTGGC TTAA

Figure 1

1 GAATTCCGCA AGGAgcacac ccggctgtcc acctgCTGCA GAGATGGTGC
upstream primer
51 ACGCAACCTC CCCGCTGCTG CTGCTGCTGC TGCTCAGCCT GGCTCTGGTq
cc t original sequence
101 gctcccgga tccctgcccag AAAGTGCTCG CTGACTGGGA AATGGACCAA
mutagenic primer
151 CGATCTGGGC TCCAACATGA CCATCGGGGC TGTGAACAGC AGAGGTGAAT
201 TCACAGGCAC CTACATCACA GCCGTAACAG CCACATCAAA TGAGATCAAA
251 GAGTCACCAC TGCATGGAC ACAAAACACC ATCAACAAGA GGACCCAGCC
301 CACCTTGCG TTCACCGTCA ATTGGAAGTT TTCAGAGTCC ACCACTGTCT
351 TCACGGGCCA GTGCTTCATA GACAGGAATG GGAAGGAGGT CCTGAAGACC
401 ATGTGGCTGC TGCAGTCAAG TGTAAATGAC ATTGGTGATG ACTGGAAAGC
451 TACCAAGGGTC GGCATCAACA TCTTCACTCG CCTGCGCACA CAGAAGGAGT
501 GAGGATGGCC CCGCAAAGCC AGCAACAATG CCGGAGTGCT GACACTGCTT
551 GTGATATTCC TCCCCAATAA AGCTTG
+ Hind III

Figure 2

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ECOR I
↓
1 GAATTCTGCAT ATGGCTGAAG CTGGTATCAC CGGTACTTGG TACAACCAGC
51 TGGGGTCTAC CTTCATCGTT ACCGCTGGTG CTGACGGTGC ACTGACCGGT
101 ACTTACGAAA GCGCTGTTGG TAACGCTGAA AGCCGTTATG TTCTGACCGG
151 TCGTTACGAC TCTGCTCCGG CTACCGACGG TTCTGGTACT GCTCTGGGTT
201 GGACCGTTGC TTGGAAAAAC AACTACCGTA ACGCTCACTC TGCTACCACC
251 TGGTCTGGCC AGTACGTTGG TGGTGTGAA GCTCGTATCA ACACCCAGTG
301 GCTGCTGACC TCTGGTACCA CCGAAGCTAA CGCTTGGAAA TCTACCCTGG
351 TTGGTCACGA CACGTTCAACC AAAGTTAAC CGTCTGCTGC TTCTATCTAGA
↑
Xba I

Figure 3

Sal I altered Bam H I*

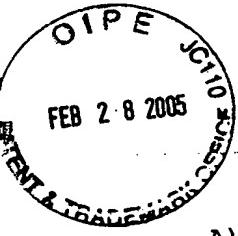
| |
----- pUC 19

|
Xba I

1 ATGGATGTTCA CAAGGAAGT TAATTCGTT GCTTACCTAC TAATTGTTCT
51 TGGTAAGATT TTCCTTFACT CCTTTGTTTT AAAAAATAAA AAAACAAAAA
101 AAATCTGGT TTATACATAT ATATACACAC AAGTAGTTTT ATTTTTTCC
151 TTTATATTAT ATTTGTTGTA GGAATATTTC TACTTGTAG CGTGGTGGAA
201 CATGTTGATG CGAAGATCTG TACTAAAGAA TGTGGTAATC TTGGGTTTGG
251 GATATGCCCA CGTTCAGAAG GAAGTCCGAA AAATCCCATA TGCATCAATT
301 GTTGCTCAGG CTATAAGGGT TGTAATTATT ATAGTGTGTTT CGGGAGATT
351 ATTTGCGAAG GAGAATCTGA CCTAAAAAAC CCAAAAGCTT GCCCCCTAAA
401 TTGTGATACA AATATTGCCT ATTCAAGATG CCCCCATTCA GAAGGAAAAT
451 CGCTAATTAA TCCCACCGGA TGTACCACAT GTTGCACAGG GTACAAGGGT
501 TGCTACTATT TCGGTAAAAA TGGCAAGTTT GTATGCGAAG GAGAGAGTGA
551 TGAACCCAAG GCAAATATGT ACCCTGCAAT GTGA

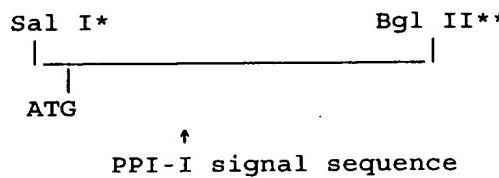
* result of PCR error during isolation of the PPI-II sequence

Figure 4

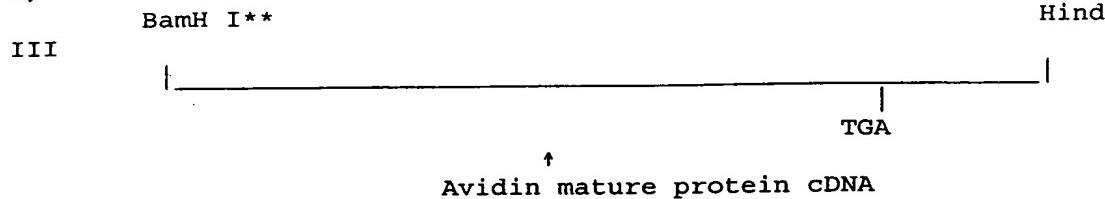


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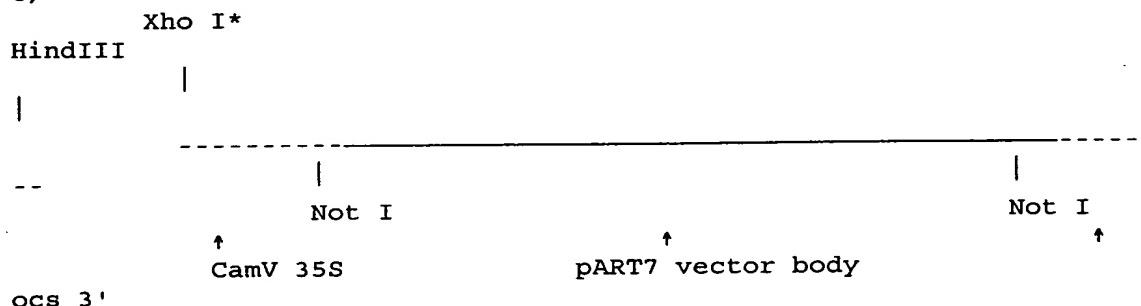
A)



B)



C)



* compatible cohesive ends
 ** compatible cohesive ends

Figure 5



Application Serial No. 09/743,690 - Filed: May 11, 2001
Inventors: Christeller *et al.* - Attorney Docket No.: 020809-000100US
Replacement Sheet

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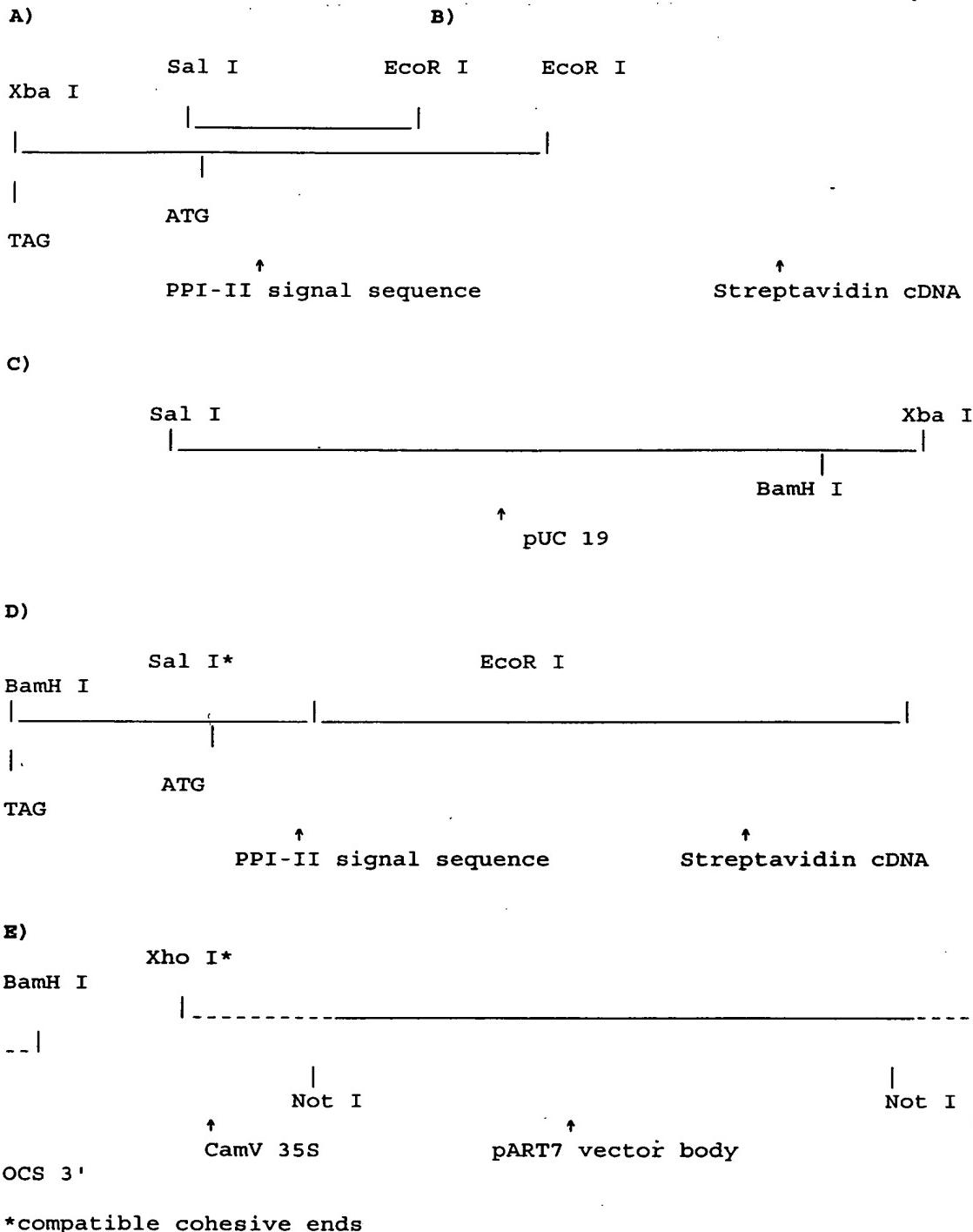
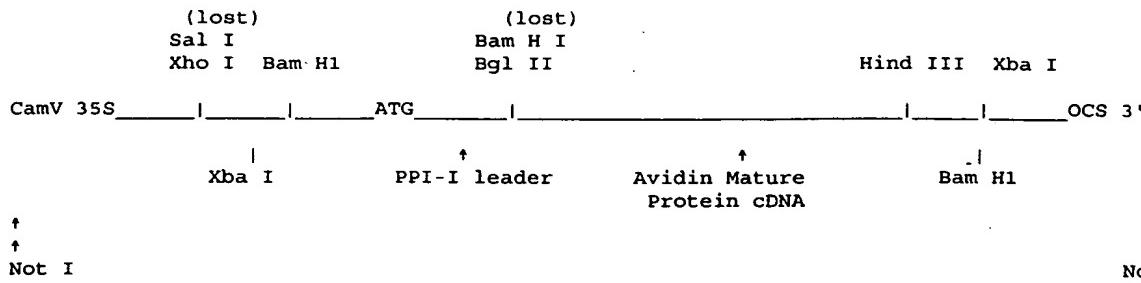


Figure 6



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A)



B)

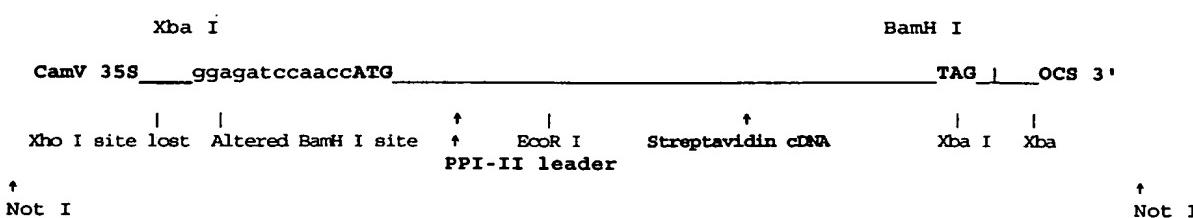


Figure 7

A)

1 ATGGAGTCAGTTTGCTCA CATCATTGTT TTCTTCTTC TTGCAACTCC
 51 CTTTGAAACT CTCTTGGCAC GAAAAGAAAAG TGATGGACCA GAGATCCCTG
 101 CCAGAAAGTG CTCGCTGACT GGGAAATGGA CCAACGATCT GGGCTCCAAC
 151 ATGACCACATCG GGGCTGTGAA CAGCAGAGGT GAATTCACAG GCACCTACAT
 201 CACAGCCGTA ACAGCCACAT CAAATGAGAT CAAAGAGTCAG CCATTGCATG
 251 GGACACAAAAA CACCACAAAC AAGAGGACCC AGCCCACCTT TGGCTTCACC
 301 GTCAATTGGA AGTTTCAGA GTCCACCACT GTCTTCACGG GCCAGTGCTT
 351 CATAGACAGG AATGGGAAGG AGGTCTGAA GACCATGTGG CTGCTGCGGT
 401 CAAGTGTAA TGACATTGGT GATGACTGGA AAGCTACCAAG GGTCGGCATC
 451 AACATCTTCA CTCGCCTGCG CACACAGAAG GAGTGA

B)

cleavage site
 ↓

1 MESKFAHIIIV FFLLATPFET LLARKESDGP EipARKCSLT GKWTNDLGSN
 51 MTIGAVNSRG EFTGTYITAV TATSNEIKES PLHGTQNTIN KRTQPTFGFT
 101 VNWKFSESTT VFTGQCFIDR NGKEVLKTMW LLRSSVNDIG DDWKATRVGI
 151 NIFTRLRTQK E*

Figure 8

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A)

1 ATGGATGTTCAACAGGAAGT TAATTCGTT GCTTACCTAC TAATTGTTCT
51 TGGTAAGATT TTCCCTTACT CCTTTGTTTT AAAAAATAAA AAAACAAAAA
101 AAATCTTGGT TTATACATAT ATATACACAC AAGTAGTTTT ATTTTTTCC
151 TTTATATTAT ATTTGTTGTA GGAATATTTC TACTTGTTAG CGTGGTGAA
201 CATGTTGATG CGAACGATCTG TACTAAGAAT TCGCATATGG CTGAAGCTGG
251 TATCACCGGT ACTTGGTACA ACCAGCTGGG GTCTACCTTC ATCGTTACCG
301 CTGGTGCTGA CGGTGCCTG ACCGGTACTT ACGAAAGCGC TGTTGGTAAC
351 GCTGAAAGCC GTTATGTTCT GACCGGTCGT TACGACTCTG CTCCGGCTAC
401 CGACGGTTCT GGTACTGCTC TGGGTTGGAC CGTTGCTTGG AAAAAACAAC
451 ACCGTAACGC TCACTCTGCT ACCACCTGGT CTGGCCAGTA CGTTGGTGGT
501 GCTGAAGCTC GTATCAACAC CCAGTGGCTG CTGACCTCTG GTACCACCGA
551 AGCTAACGCT TGGAAATCTA CCCTGGTTGG TCACNACACG TTCACCAAAG
601 TTAAACCGTC TGCTGCTTCT ATCTAG

B)

cleavage site

↓

1 MDVHKEVNPFV AYLLIVLGIF LLVSVVEHVD AKICTKnshM AEAGITGTWY
51 NQLGSTFIVT AGADGALTGT YESAVGNAES RYVLTGRYDS APATDGSGTA
101 LGWTVAWKNN YRNAHSATTW SGQYVGGAEEA RINTQWLTS GTTEANAWKS
151 TLVGHDTFTK VKPSAASI*

Figure 9



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September 1997

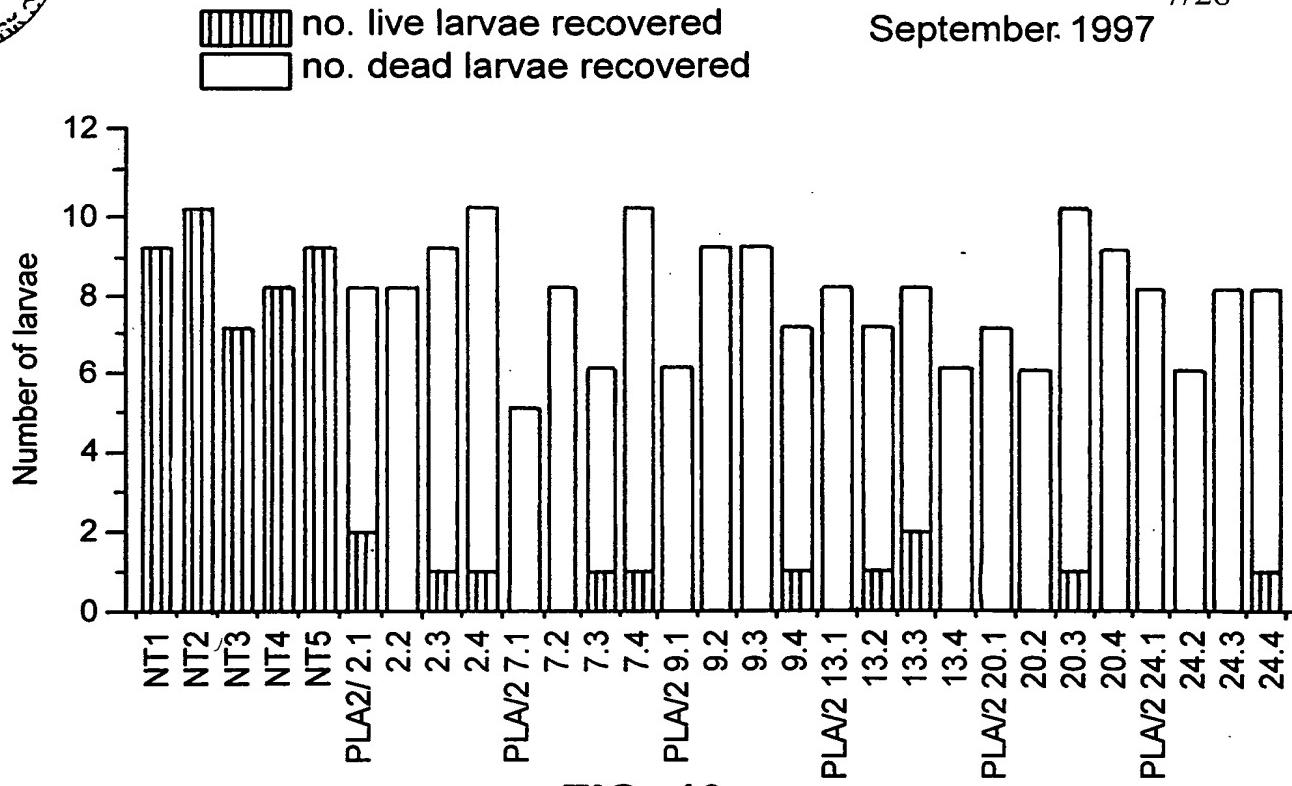


FIG. 10

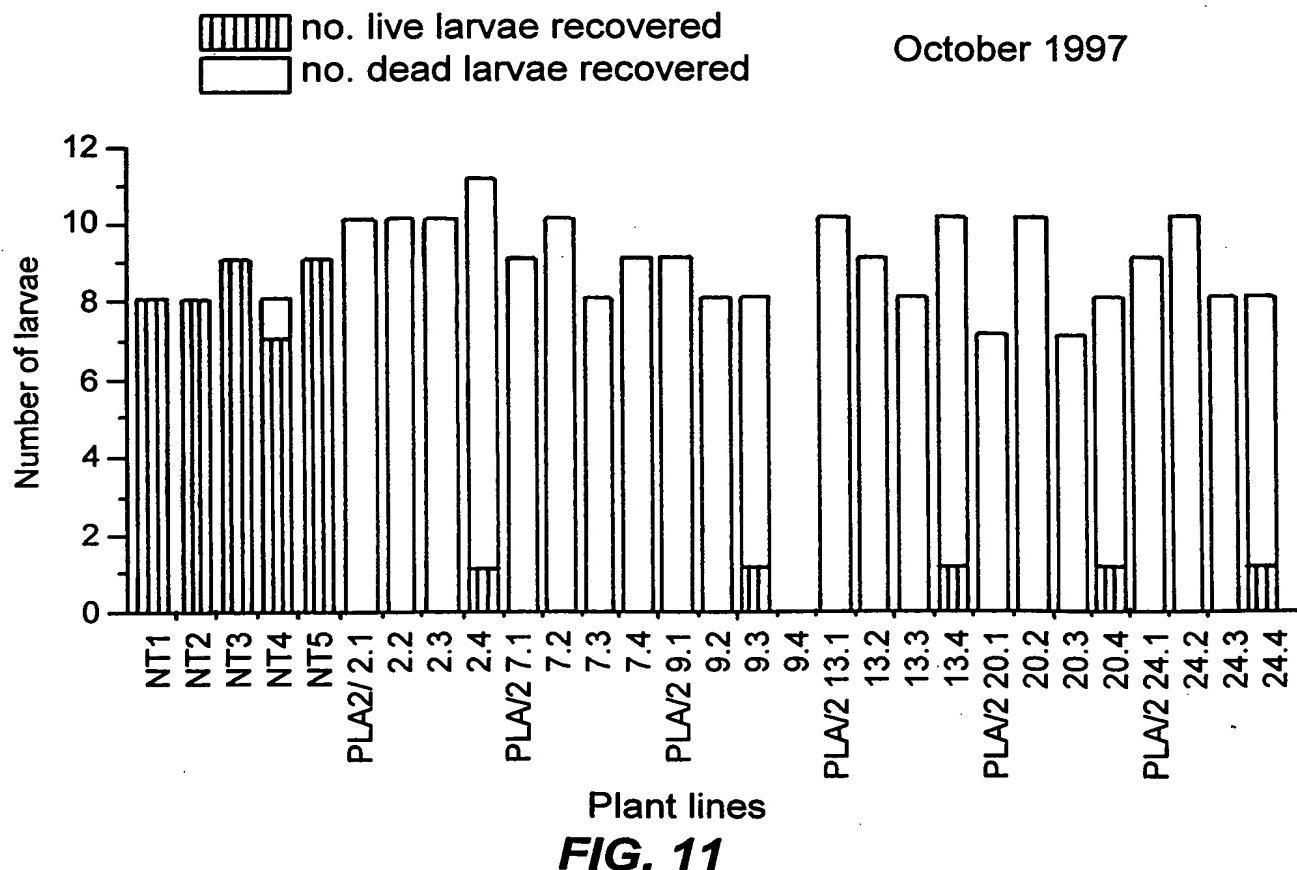


FIG. 11



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A)

1 CCCTCCGTCC CCGCCGGCA ACAACTAGGG AGTATTTTC GTGTCTCACA
51 TGC GCAAGAT CGTCGTTGCA GCCATCGCCG TTTCCCTGAC CACGGTCTCG
101 ATTACGGCCA GCGCTTCGGC AGACCCCTCC AAGGACTCGA AGGCCAGGT
151 CTCGGCCGCC GAGGCCGGCA TCACCGGCAC CTGGTACAAC CAGCTCGGCT
201 CGACCTTCAT CGTGACCGCG GGC GCGCCGACG GCGCCCTGAC CGGAACCTAC
251 GAGTCGGCCG TCGGCAACGC CGAGAGCCGC TACGT CCTGA CCGGTCGTTA
301 CGACAGCGCC CCGGCCACCG AC GG CAGCGG CACCGCCCTC GGTTGGACGG
351 TGGCCTGGAA GAATAACTAC CGCAACGCC ACTCCGCGAC CACGTGGAGC
401 GGCCAGTACG TCGGCGCGC CGAGGCAGGG ATCAACACCC AGTGGCTGCT
451 GACCTCCGGC ACCACCGAGG CCAACGCCTG GAAGTCCACG CTGGTCGGCC
501 ACGACACCTT CACCAAGGTG AAGCCGTCCG CGCCTCCAT CGACGCGCG
551 AAGAAGGCCG GCGTCAACAA CGGCAACCCG CTCGACGCCG TTCAGCAGTA
601 GTC GCGTCCC GGCACCGCG GGTGCCGGGA CCTCGGCC

B)

1 MRKIVVAAIA VSLTTVSITA SASADPSKDS KAQSAAEAG ITGTWYNQLG
51 STFIVTAGAD GAL TGTYESA VGNAESRYVL TGRYDSAPAT DGSGTALGWT
101 VAWKNNYRNA HSATTWSQY VGGAEARINT QWL LTSGTTE ANAWKSTLVG
151 HDTFTKVVKPS AASIDAAKKA GVNNGNPLDA VQQ

Figure 12



Application Serial No. 09/743,690 - Filed: May 11, 2001
Inventors: Christeller *et al.* - Attorney Docket No.: 020809-000100US
Replacement Sheet

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Figure 13

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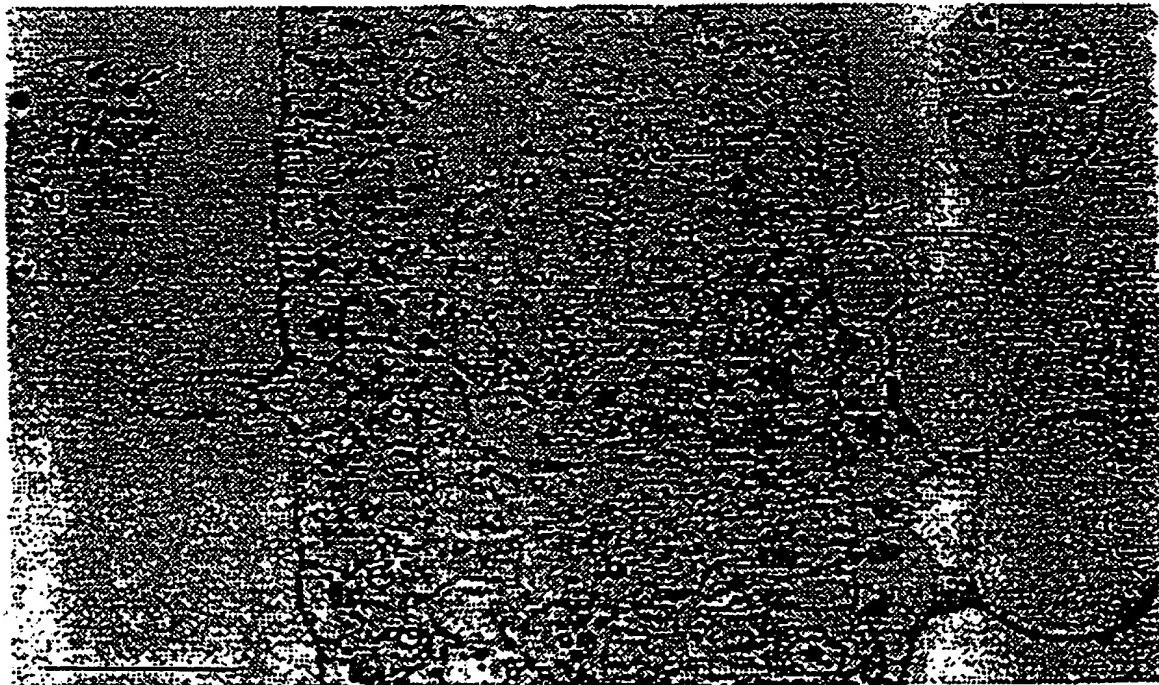


Figure 14



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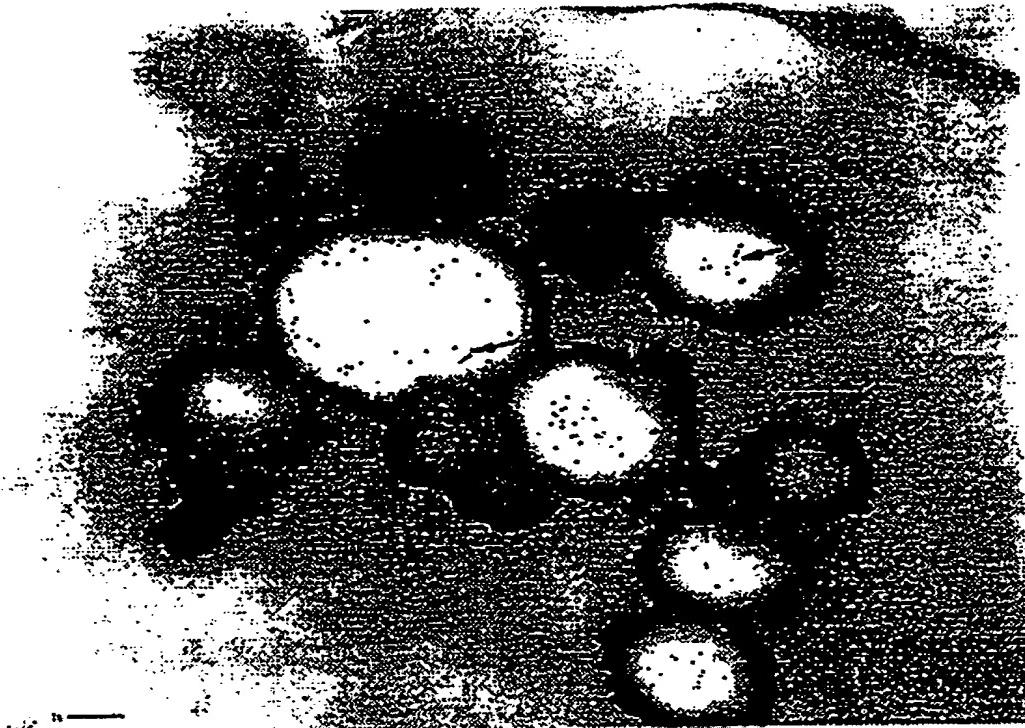


Figure 15



Figure 16

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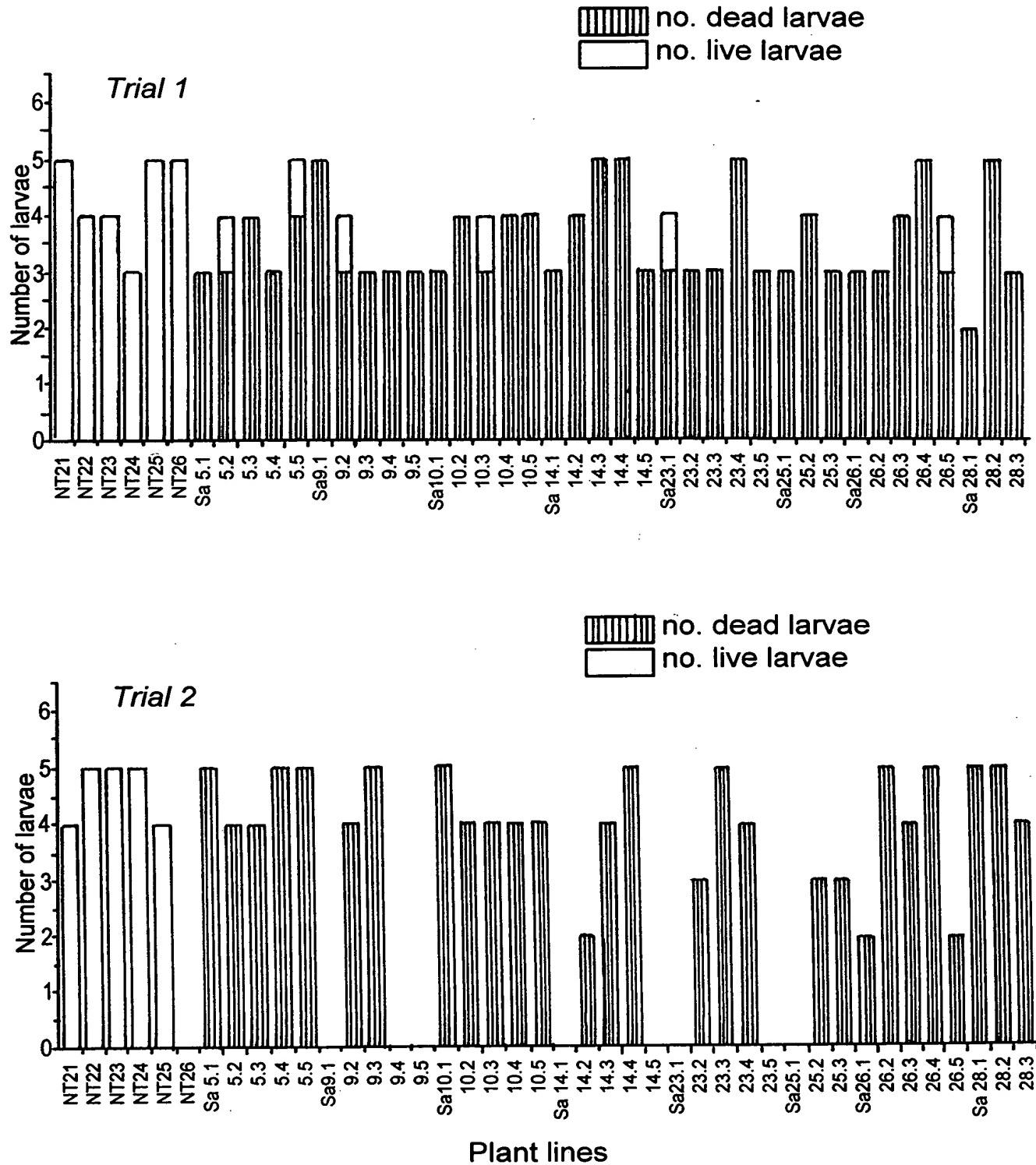


FIG. 17



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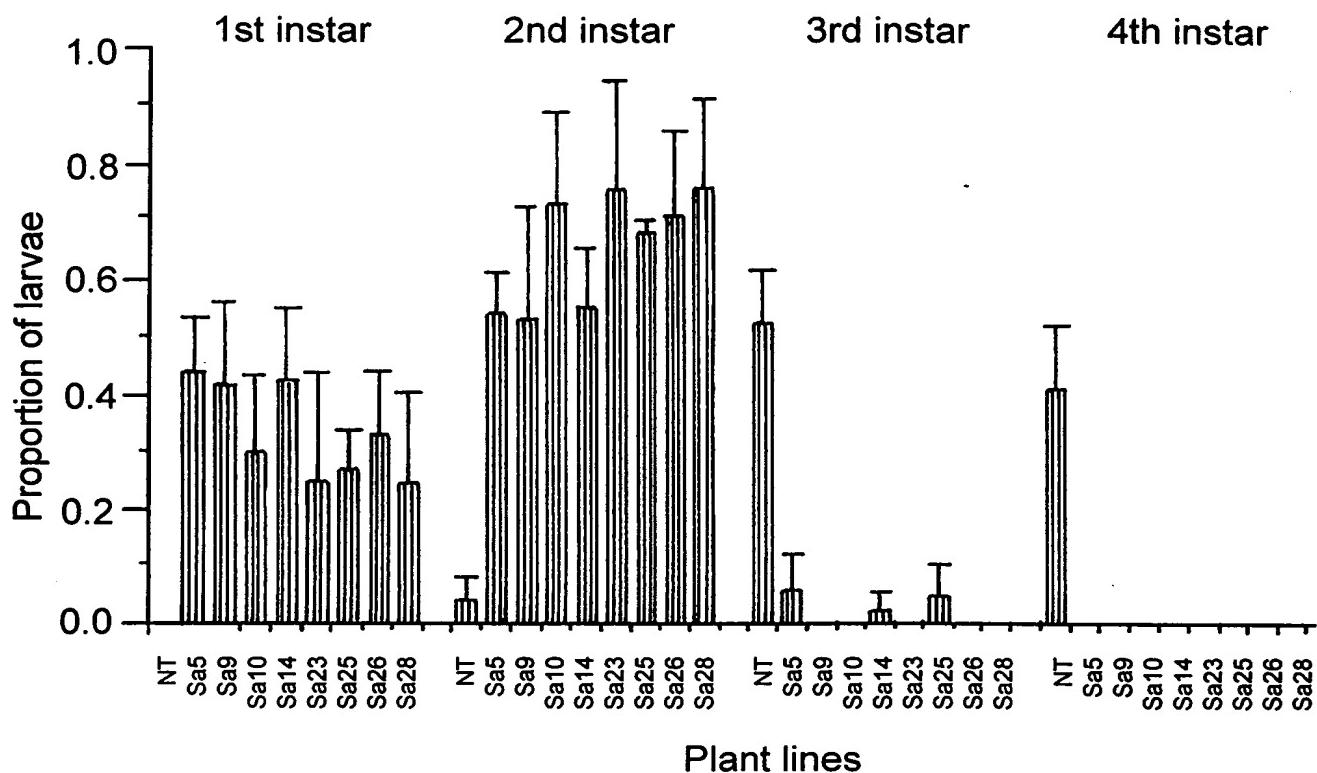


FIG. 18

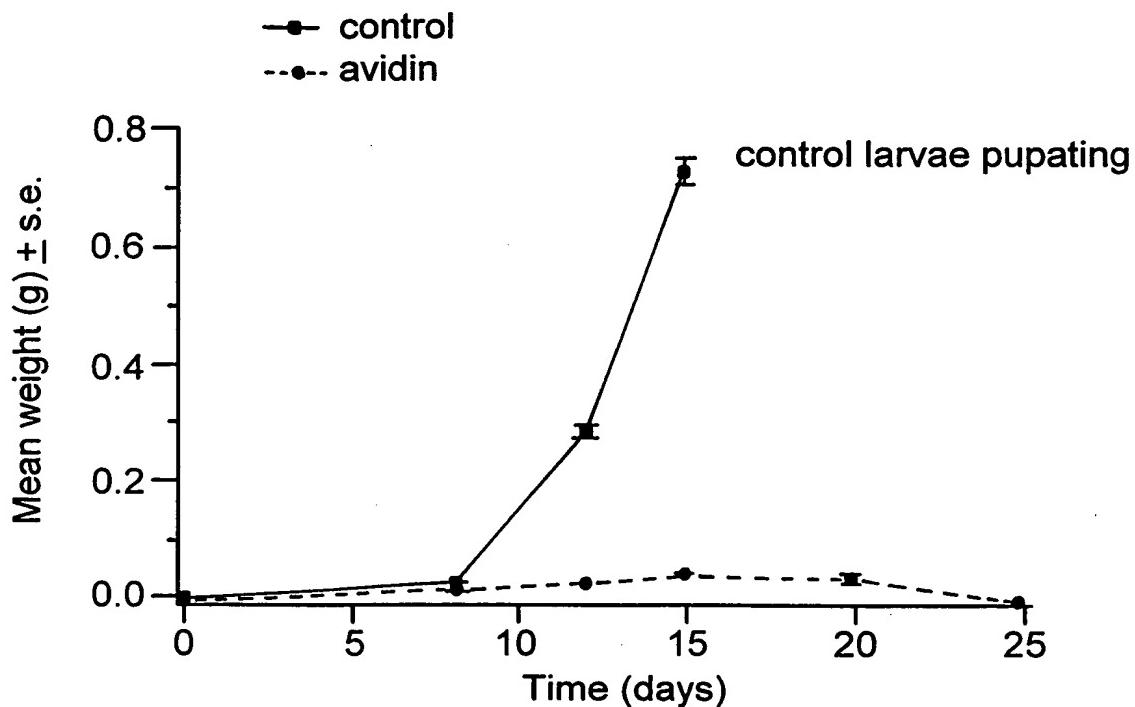


FIG. 19

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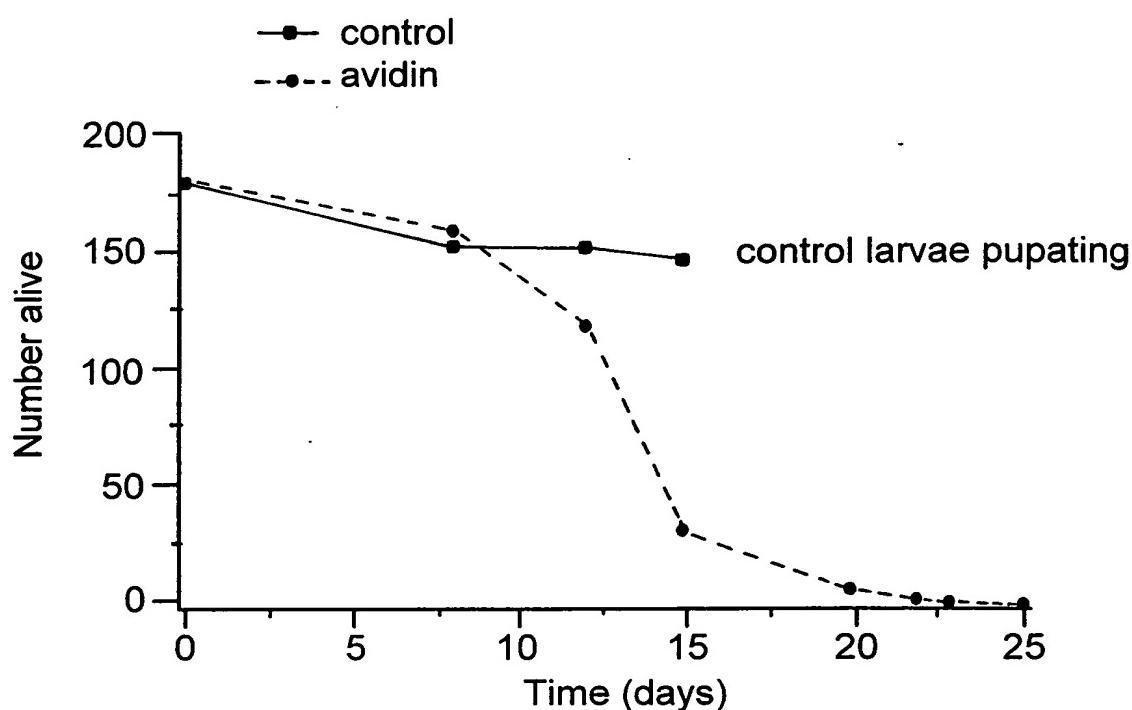


FIG. 20

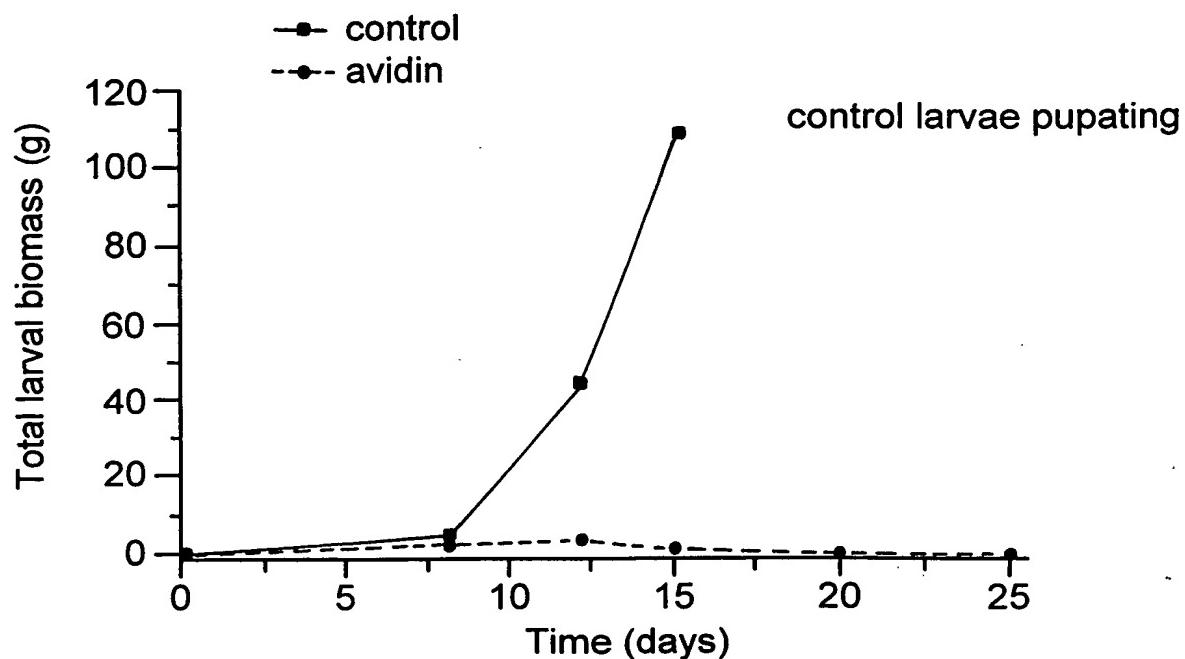


FIG. 21

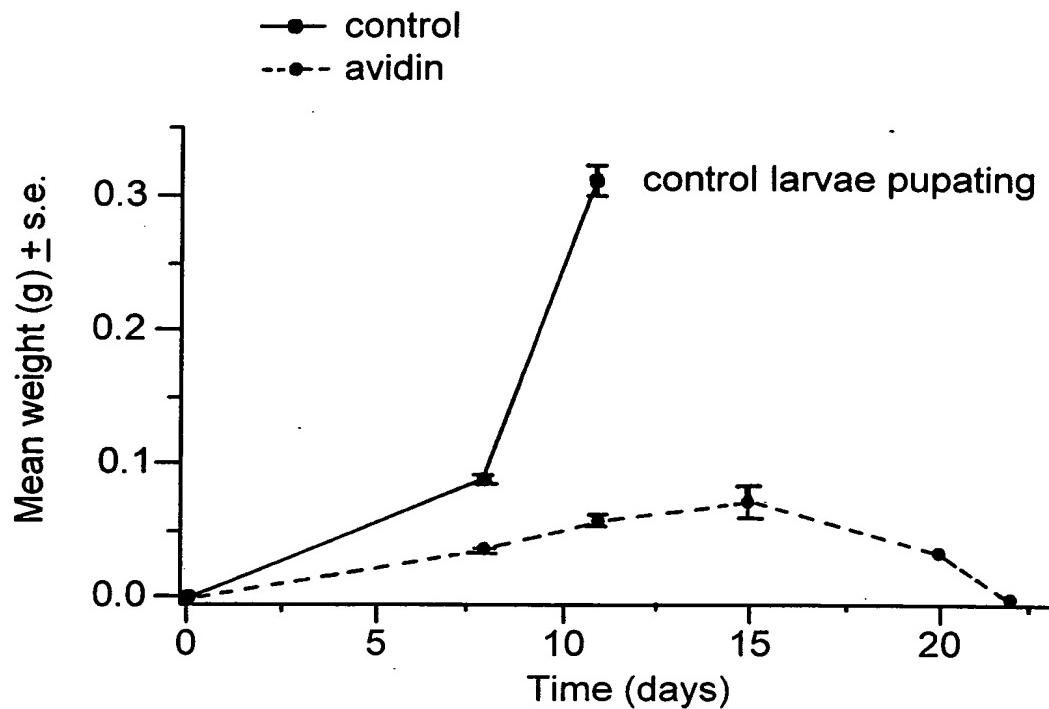


FIG. 22

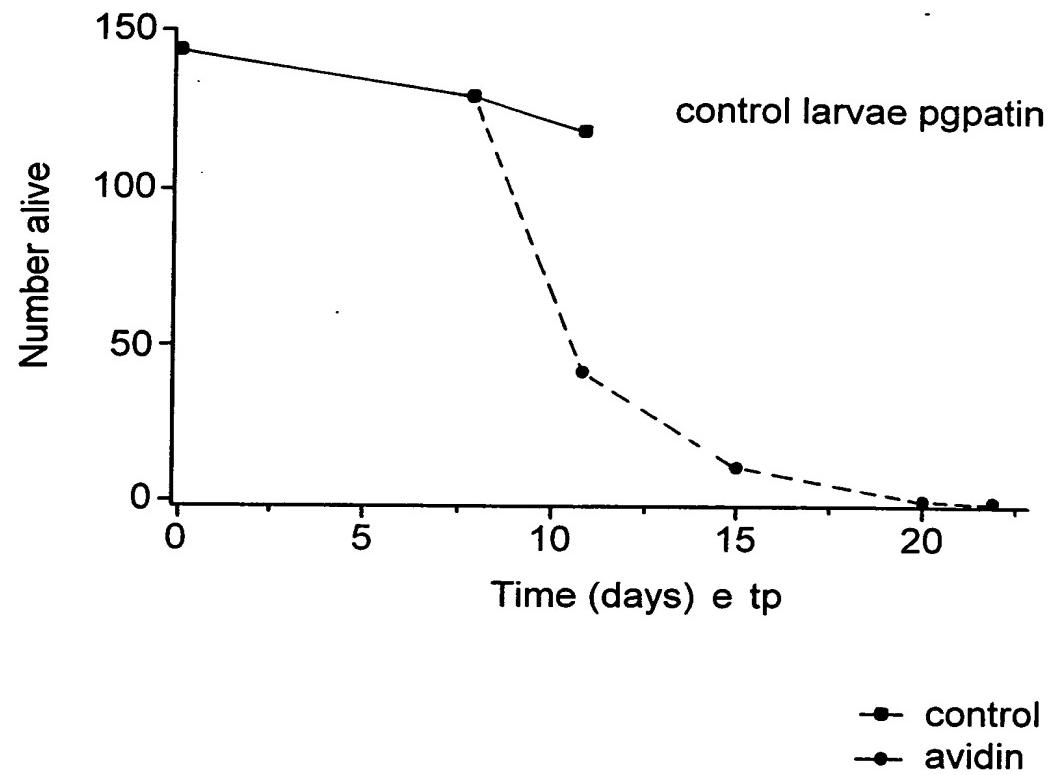


FIG. 23

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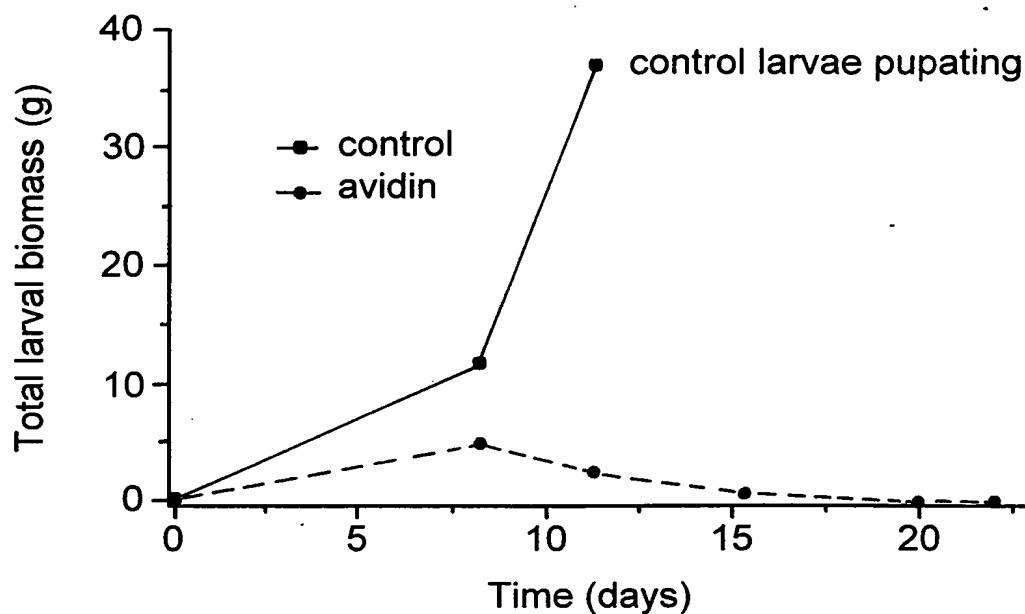


FIG. 24

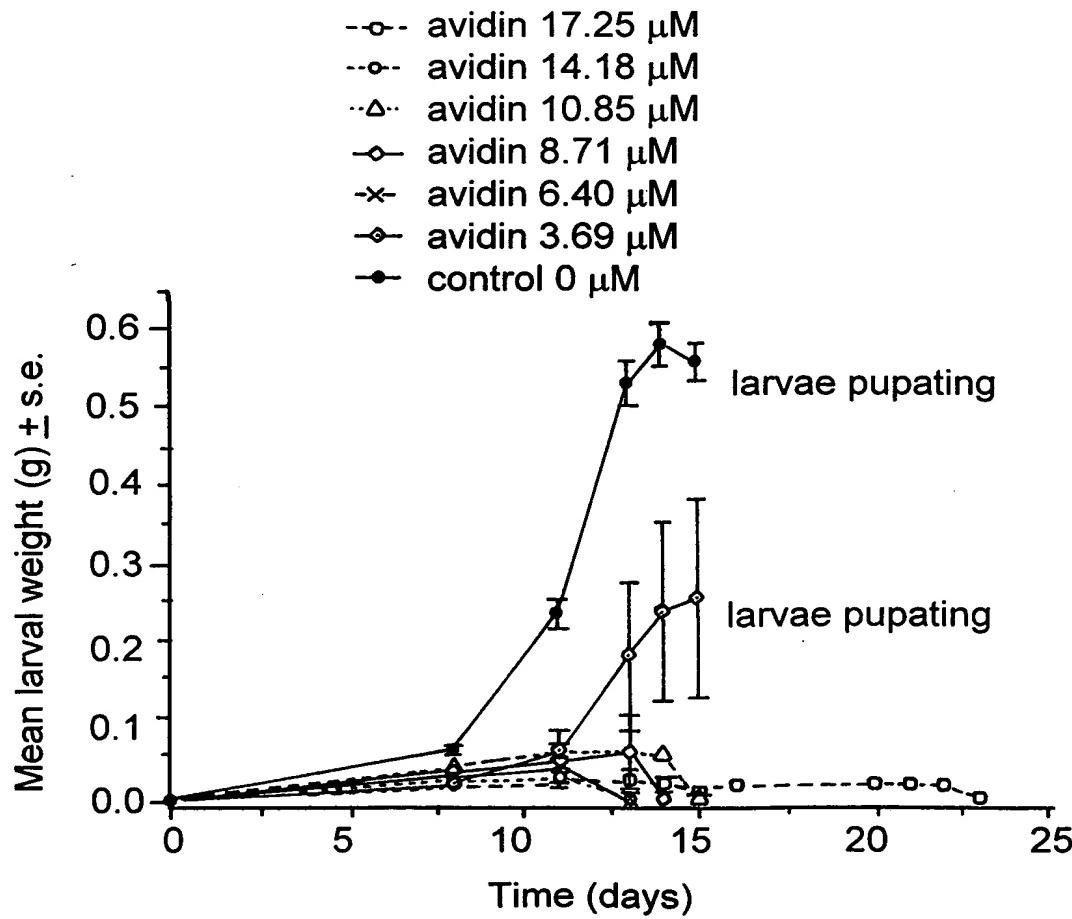


FIG. 25

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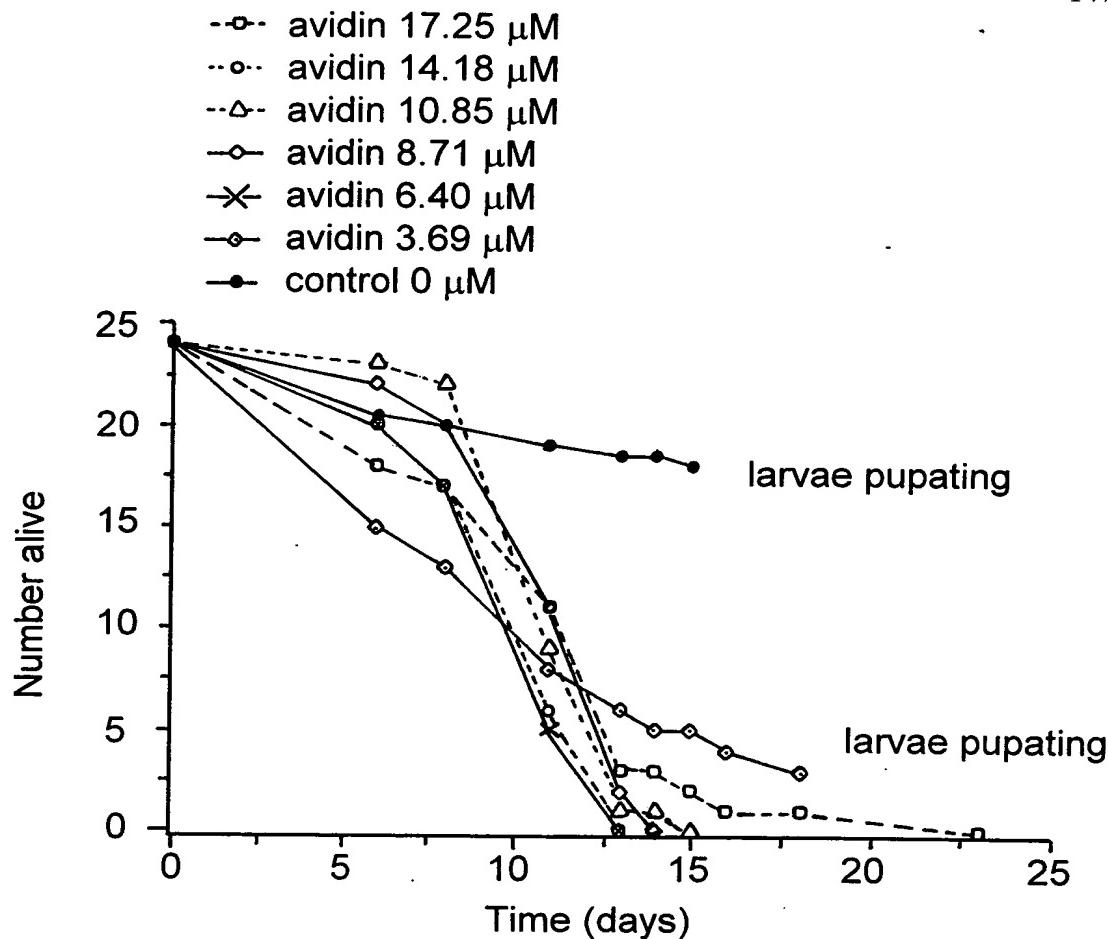


FIG. 26

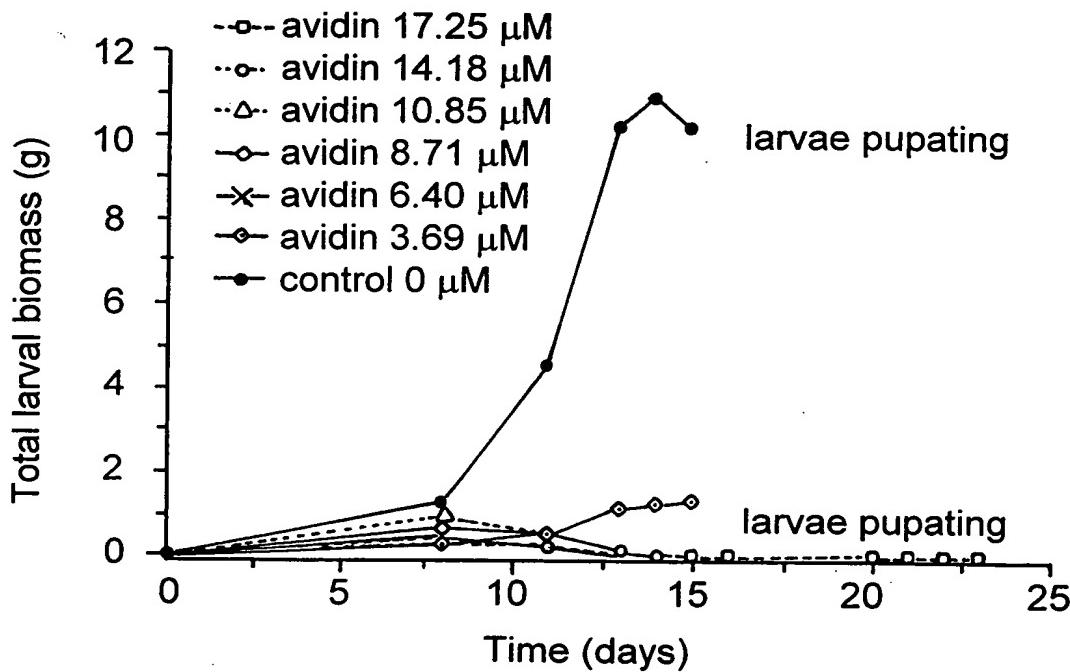


FIG. 27

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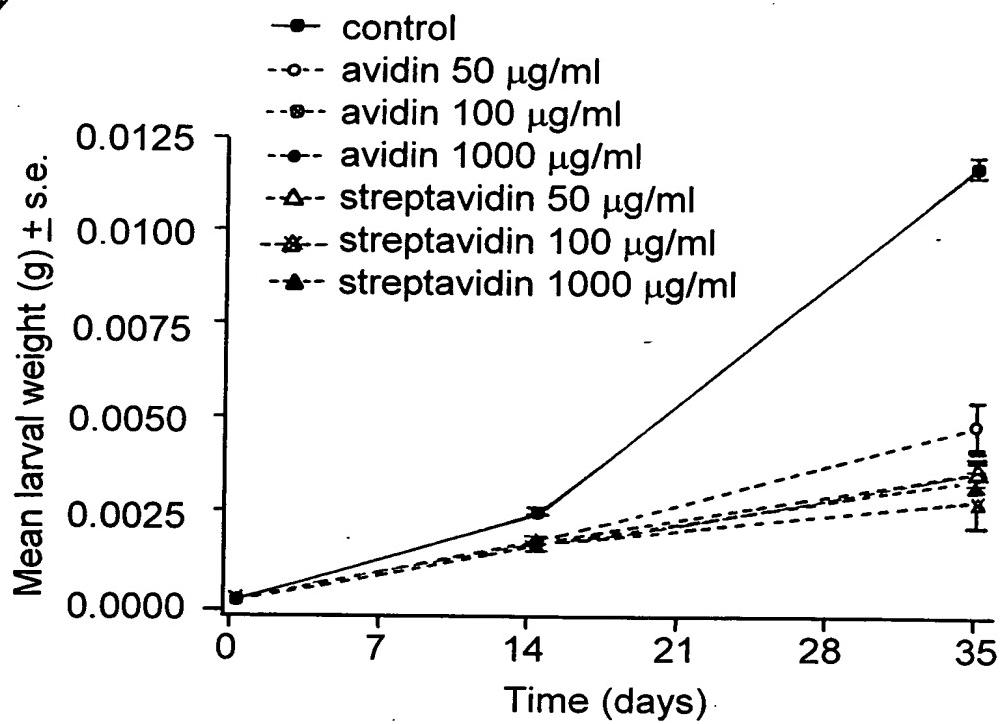


FIG. 28

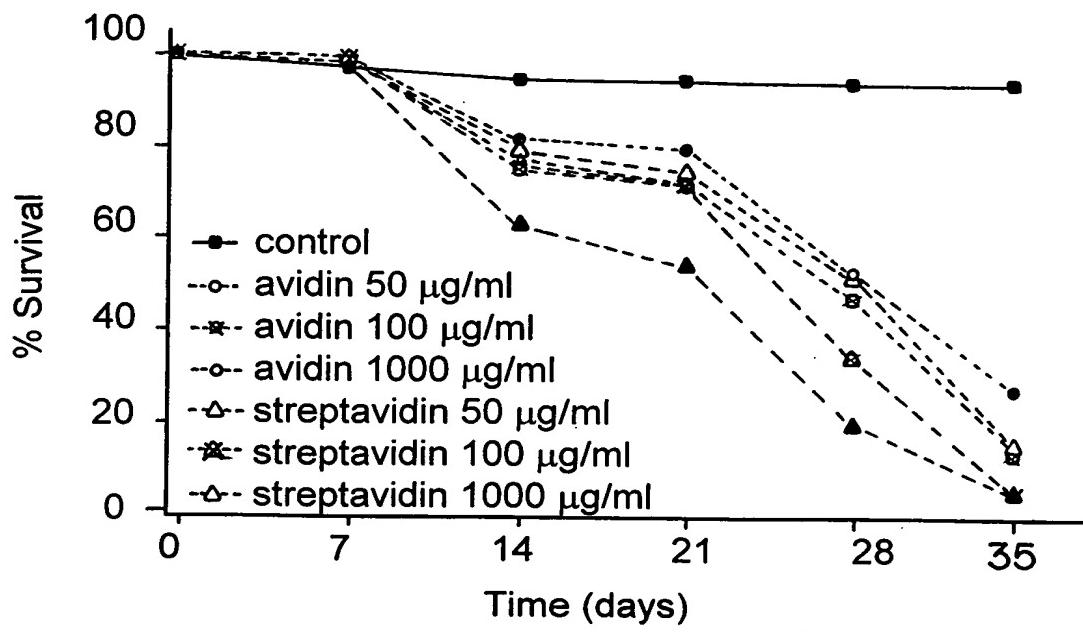


FIG. 29

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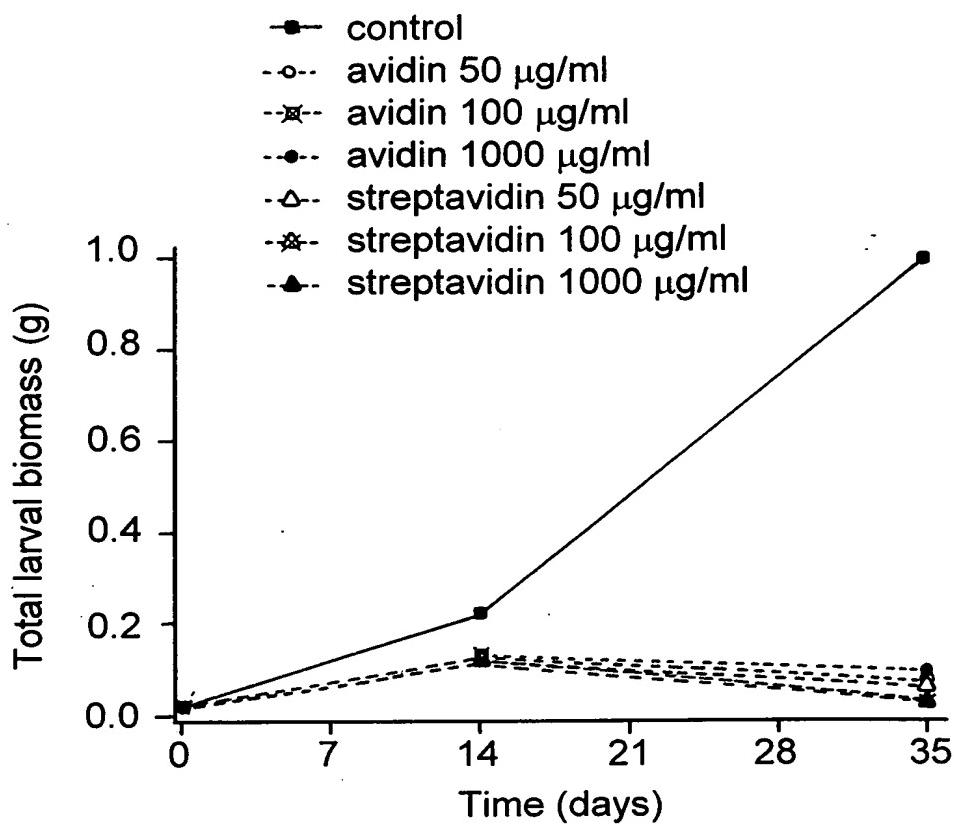


FIG. 30

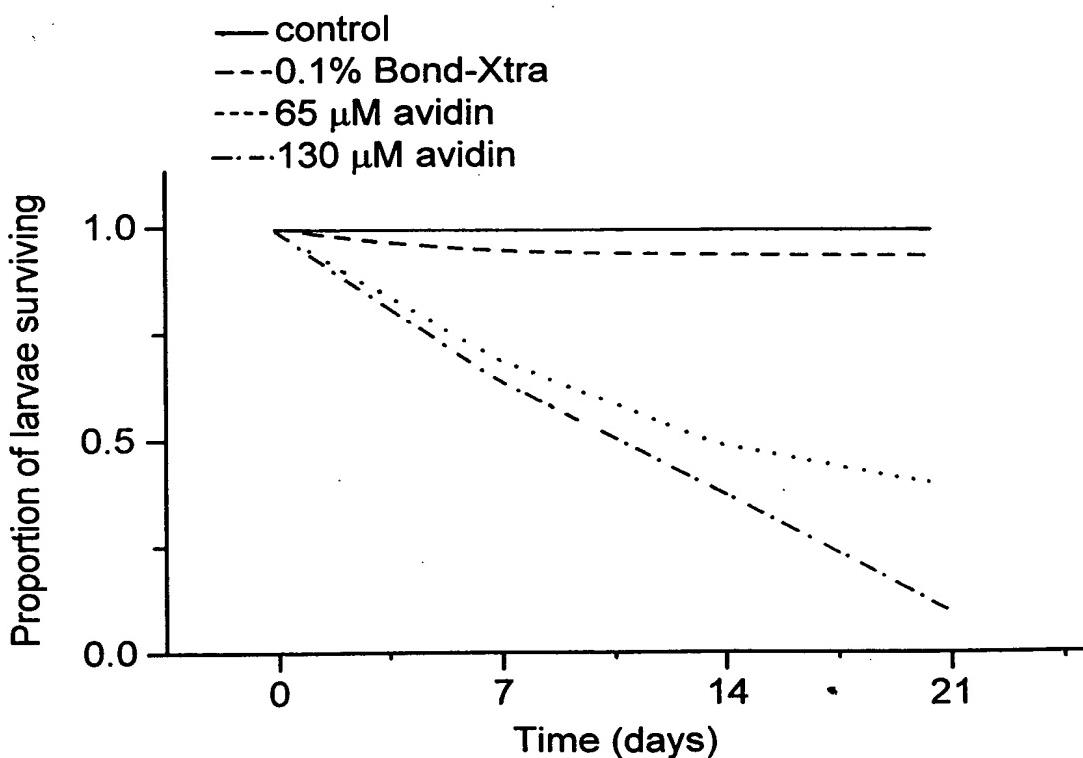


FIG. 31

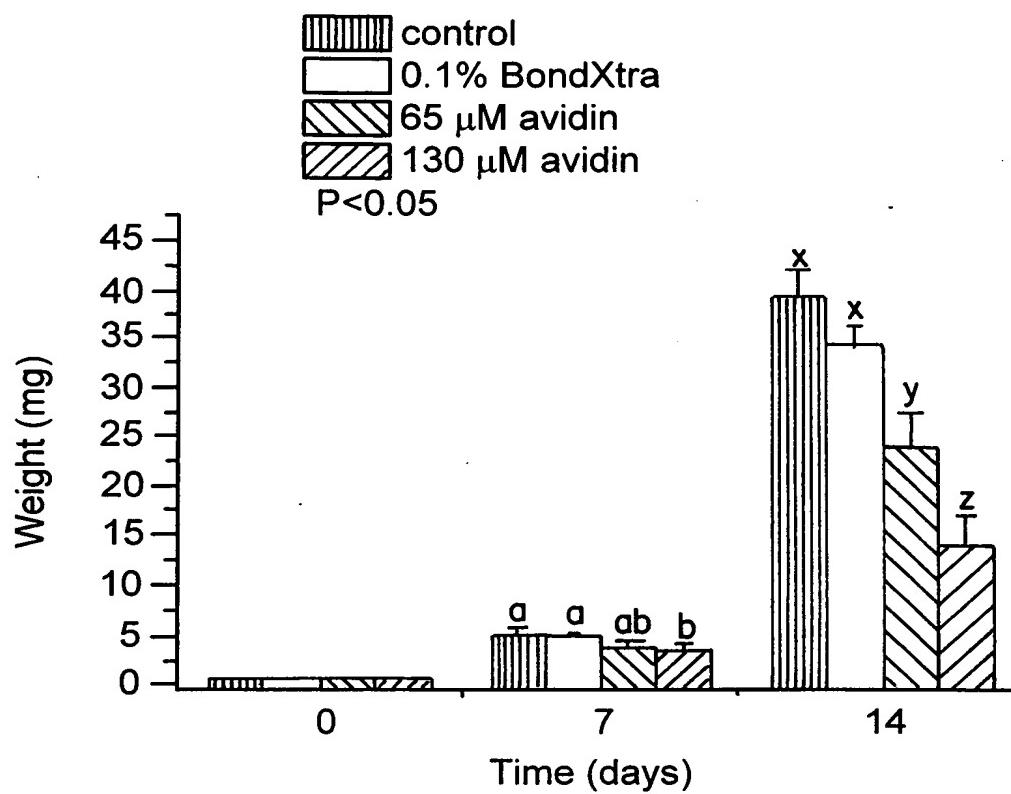


FIG. 32

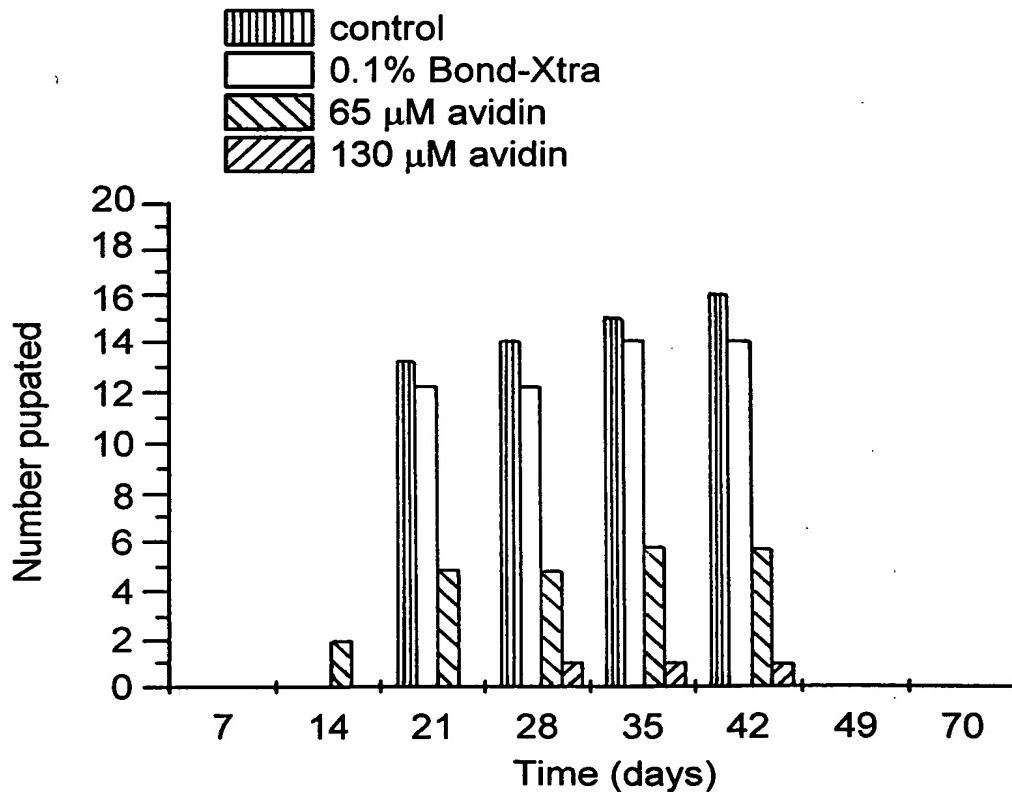


FIG. 33

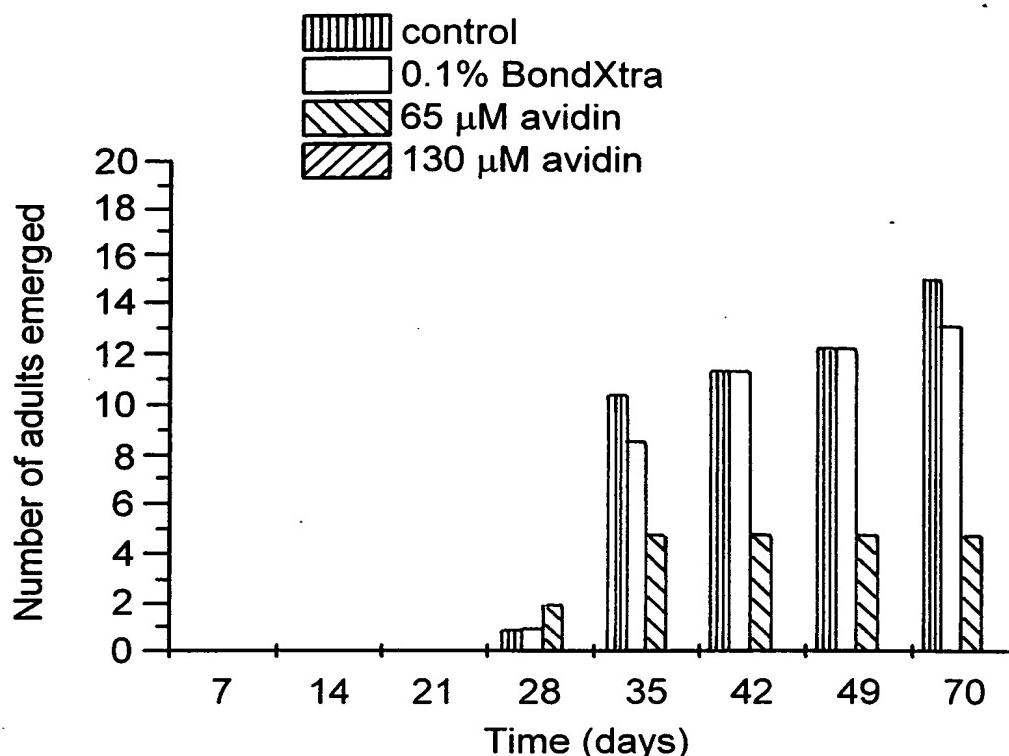
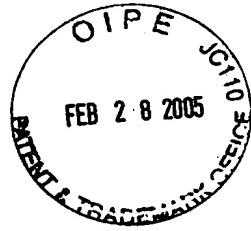


FIG. 34

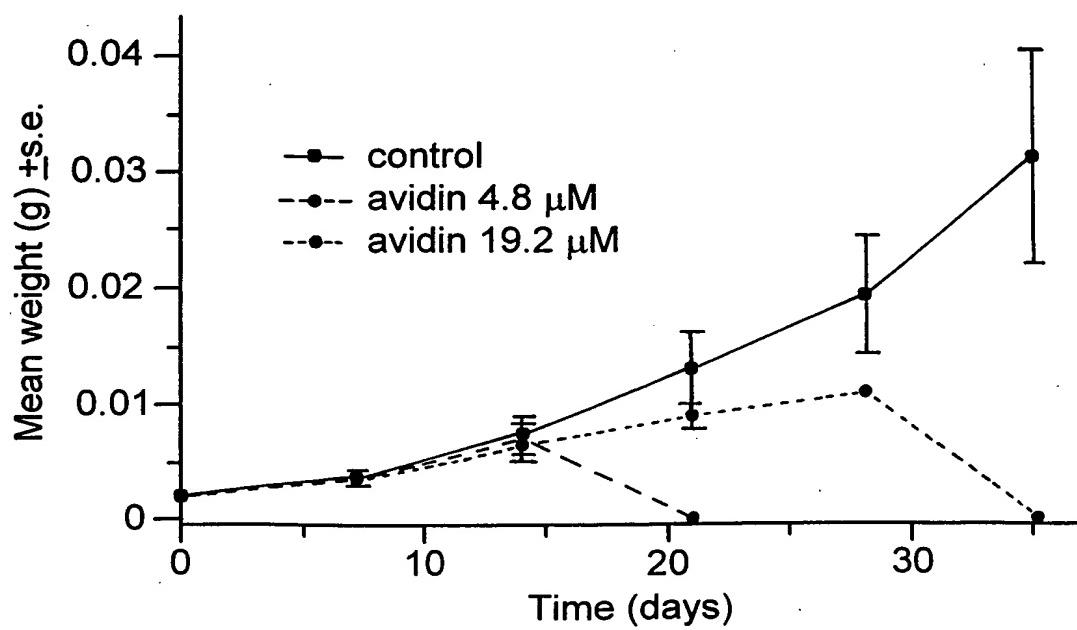


FIG. 35

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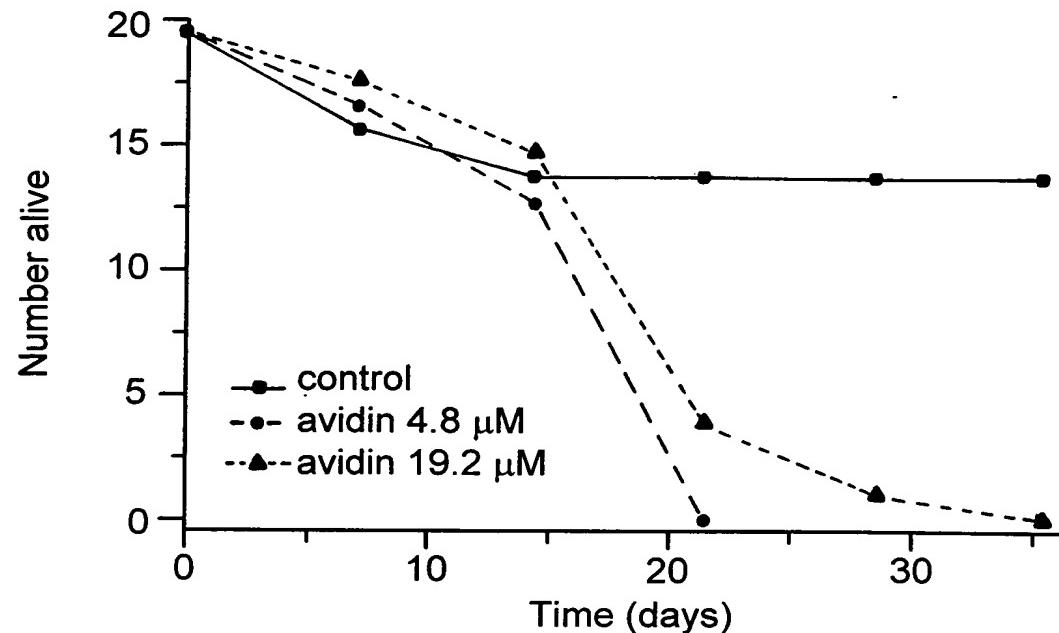


FIG. 36

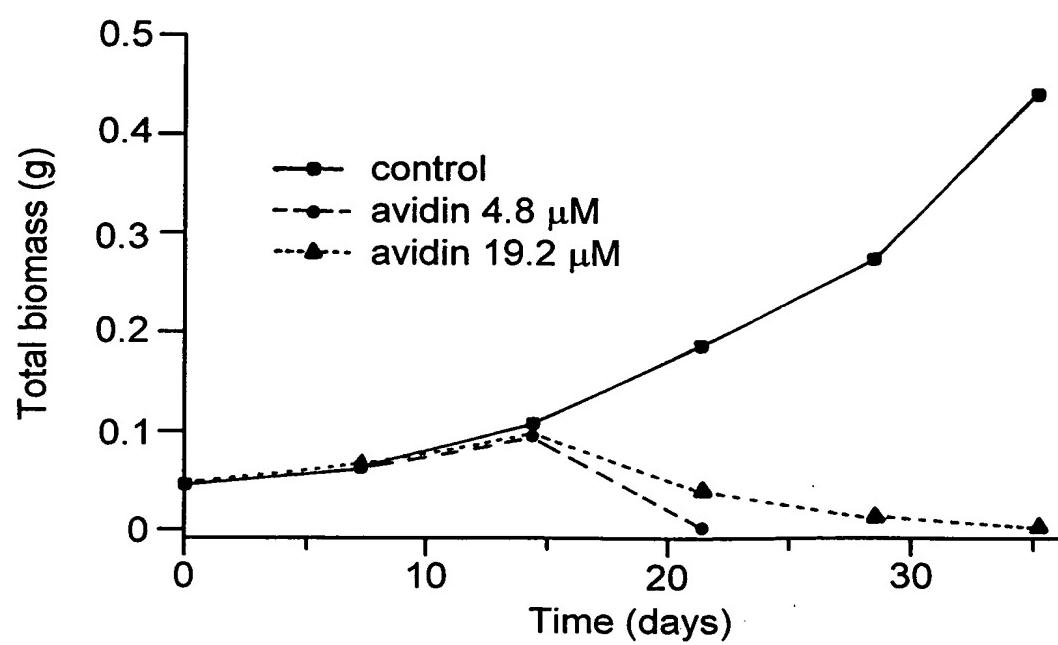


FIG. 37

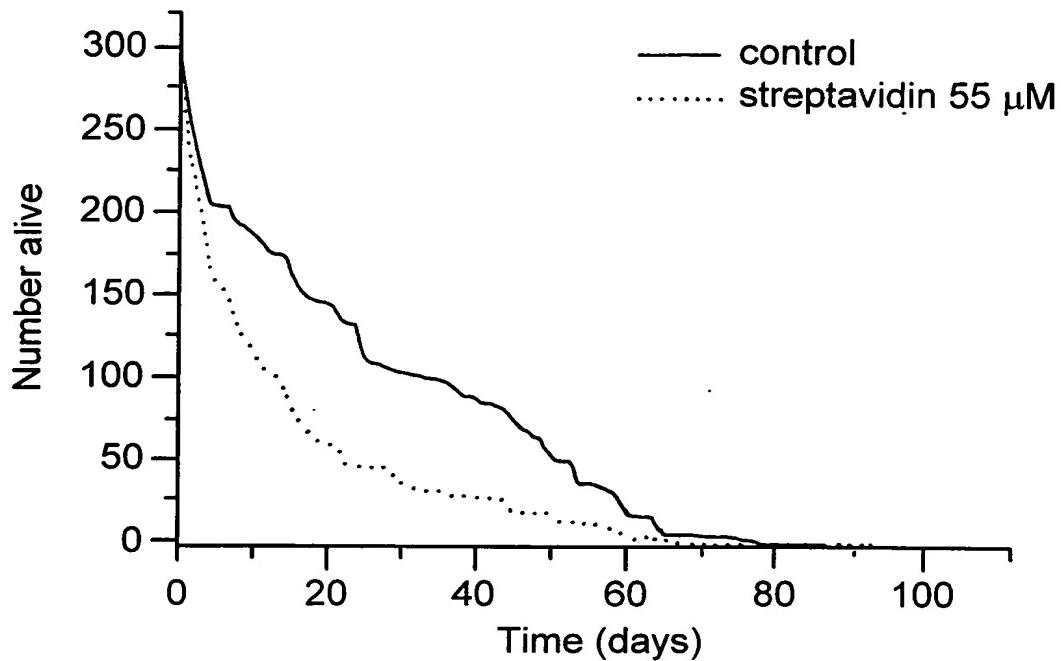


FIG. 38

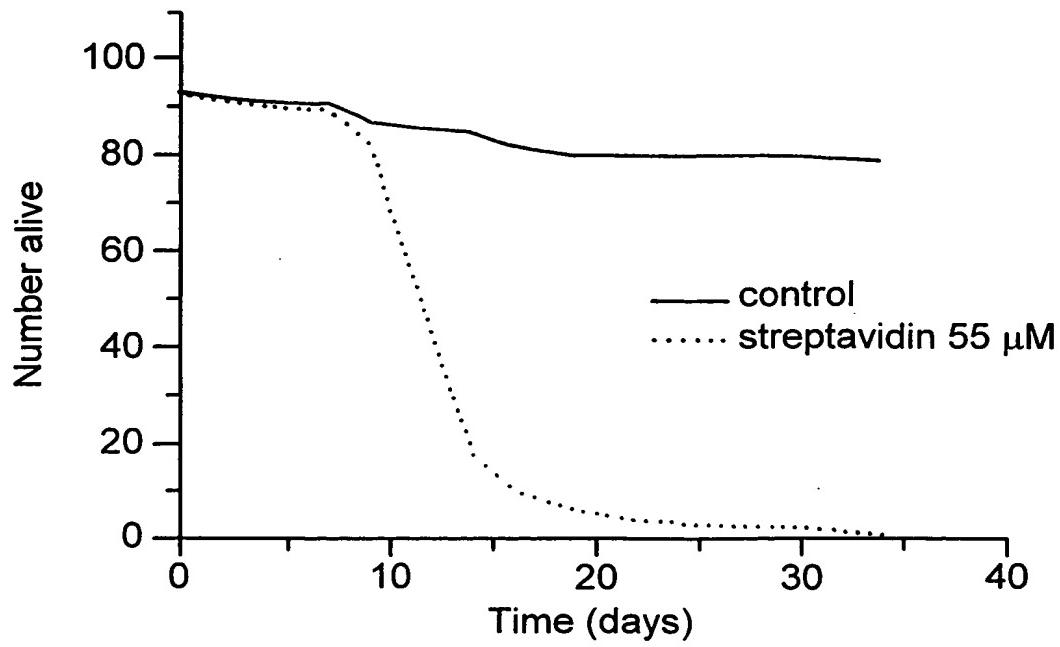


FIG. 39

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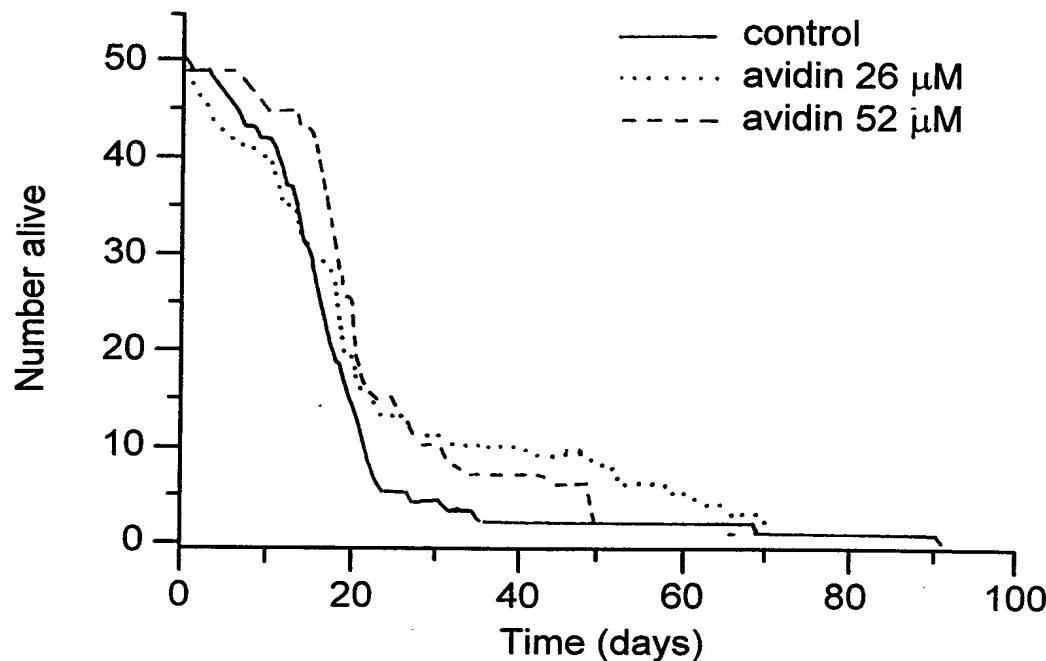


FIG. 40

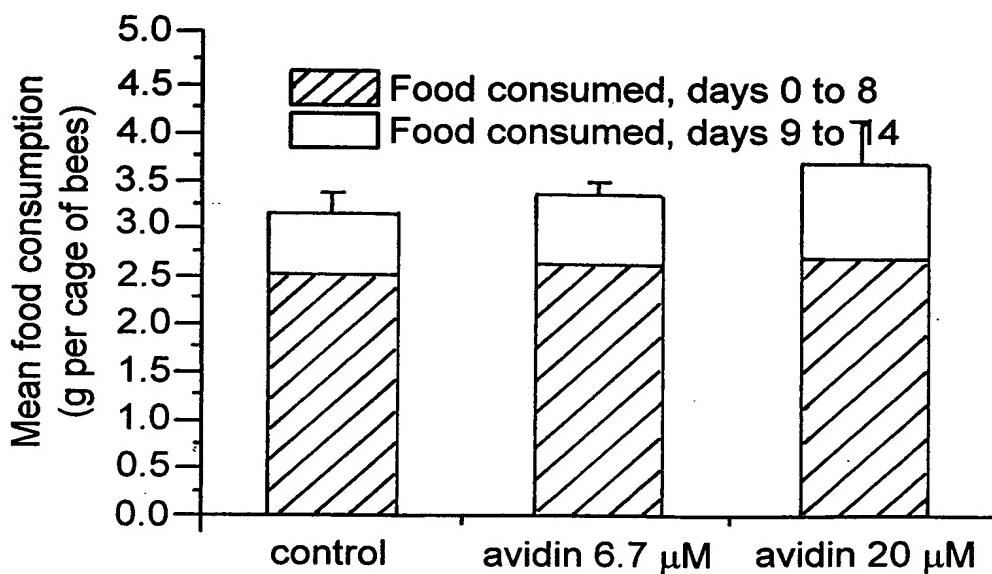


FIG. 41

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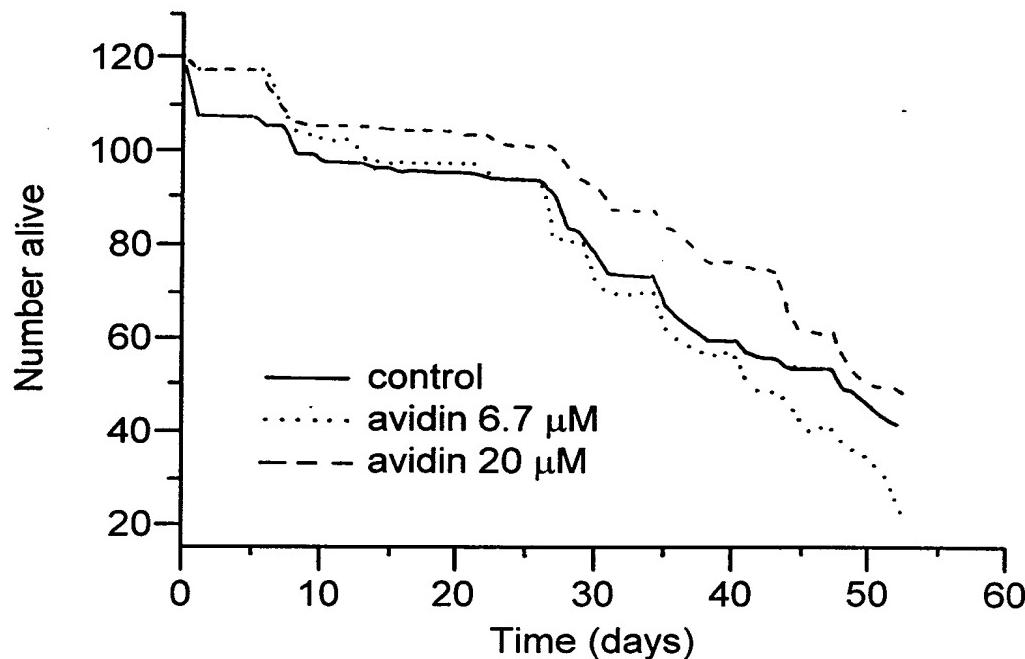


FIG. 42

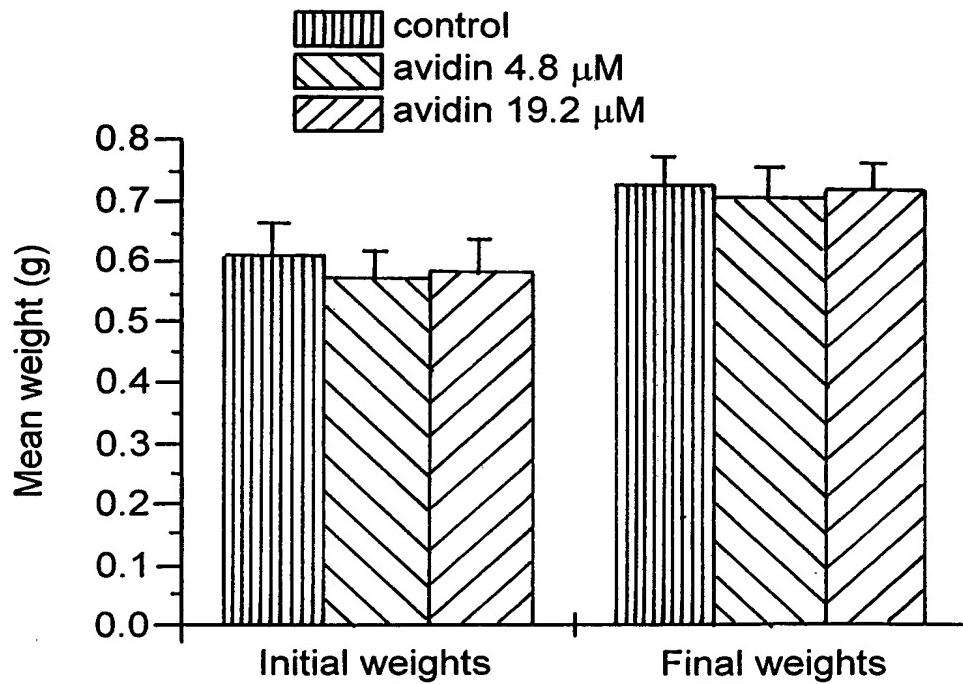


FIG. 43

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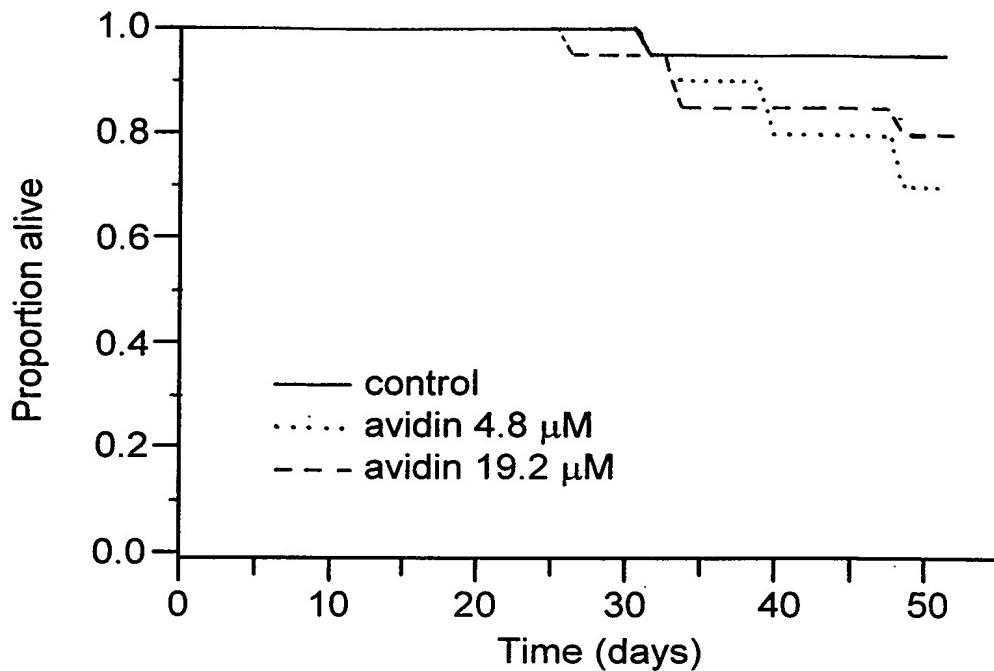


FIG. 44

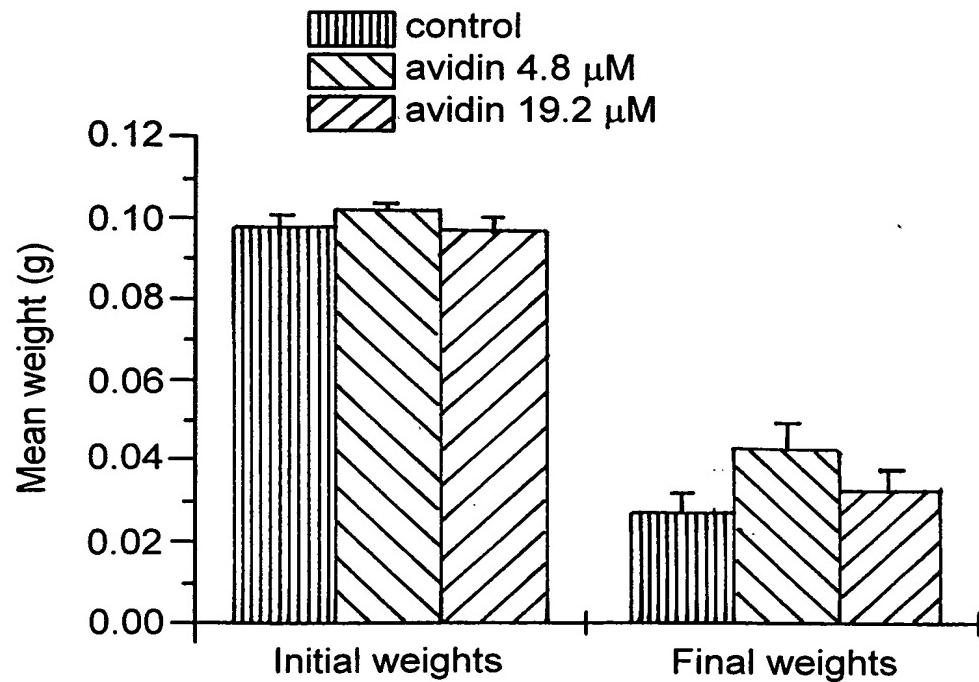


FIG. 45

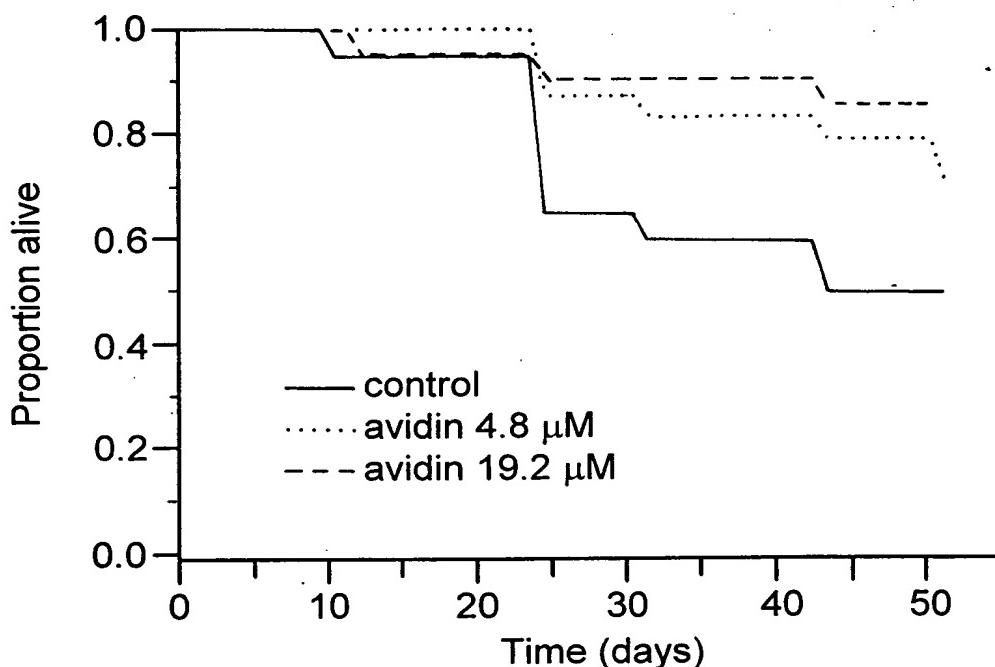


FIG. 46

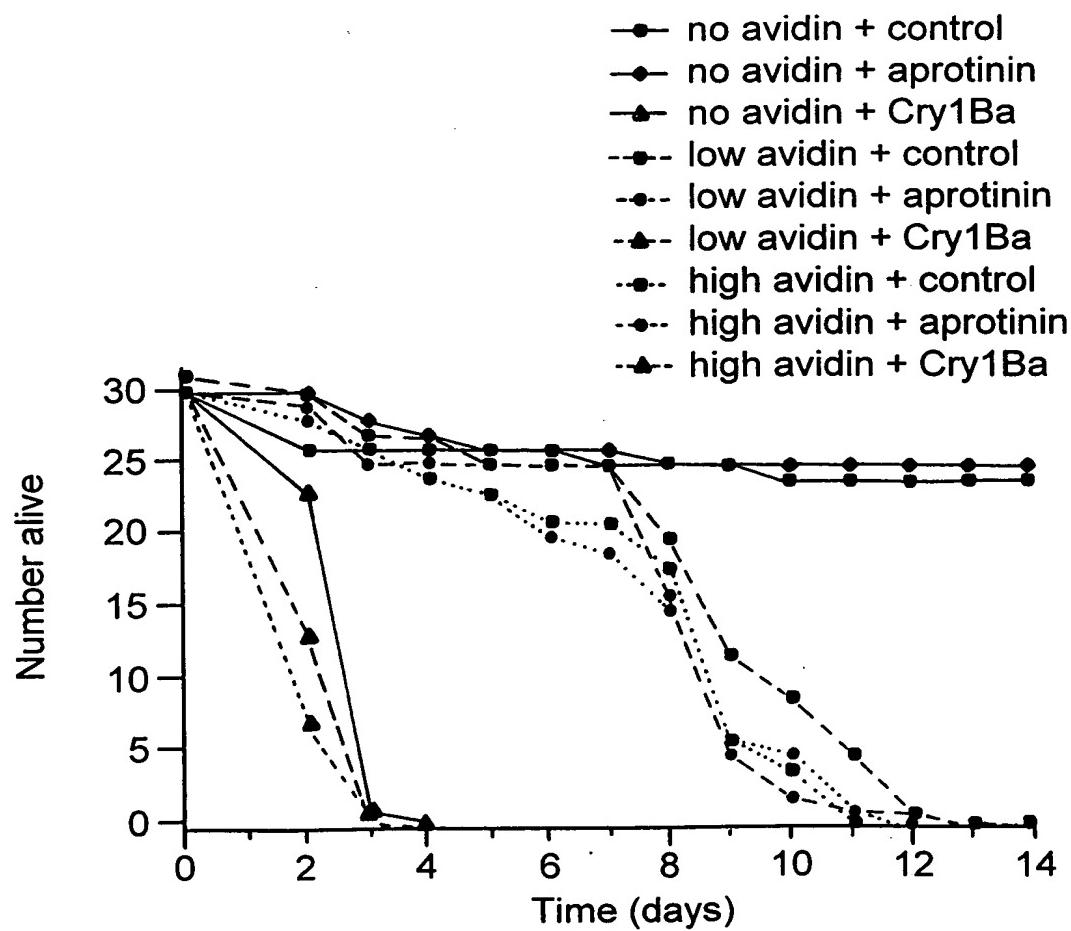


FIG. 47

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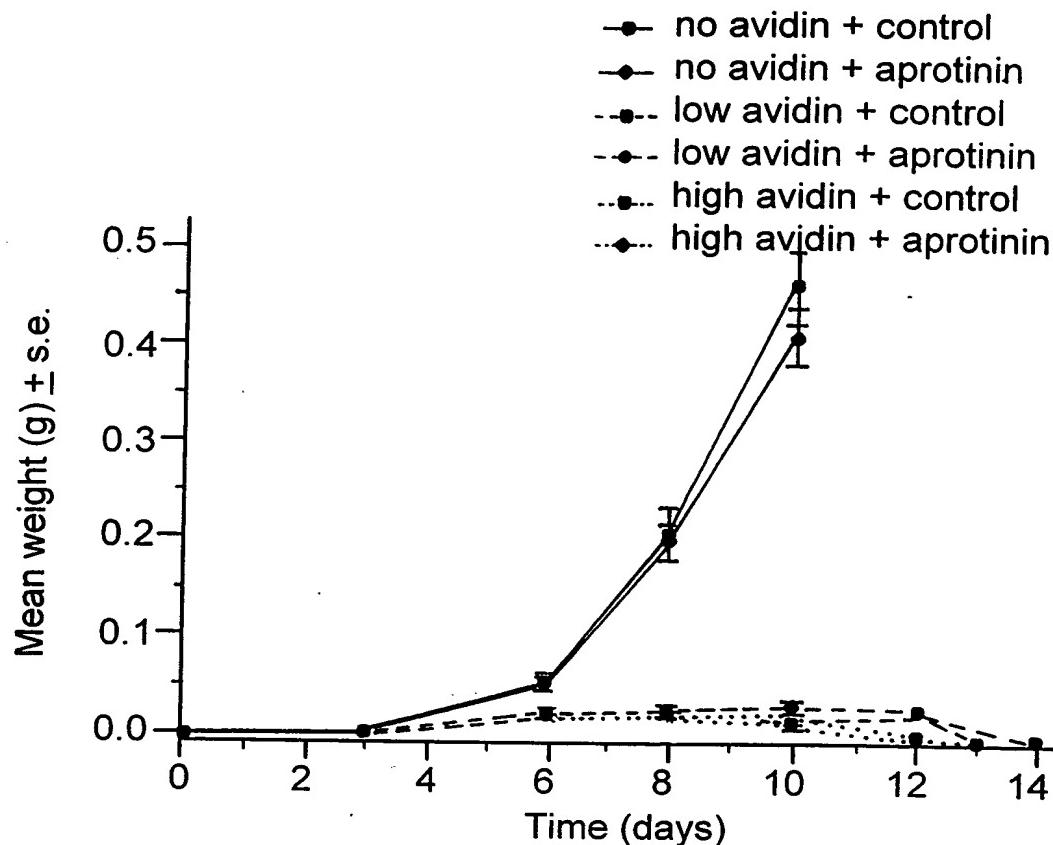


FIG. 48

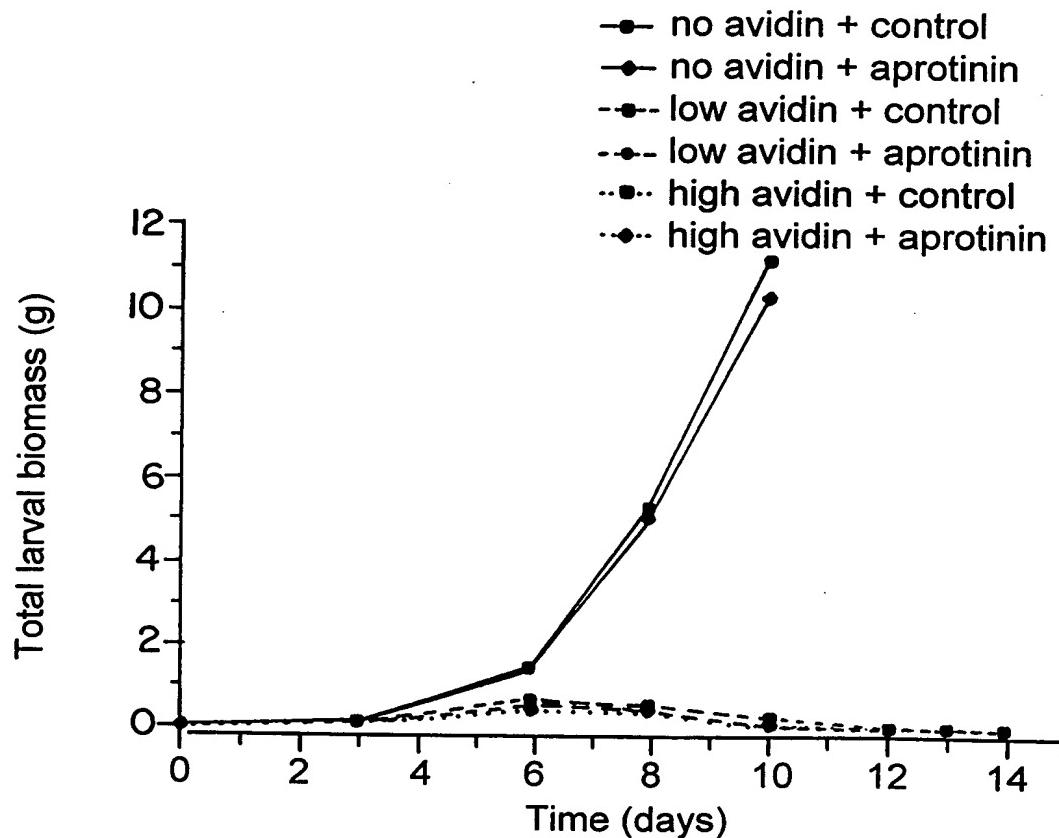


FIG. 49